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BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

SATURDAY DECEMBER 26 1959

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 26 1959

HYPERTENSION AND THE KIDNEY*

II. EXPERIMENTAL BASIS OF RENAL HYPERTENSION

BY

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In turning from the observations largely on human hypertension which I covered in my first lecture, the experimental work which has emerged in part because of this sort of observation in man must now be considered. The first important point to make is that part of the confusion in considering experimental hypertension is that so many species of animal have been used, and it is often forgotten that it is not always possible to transfer an argument based on data obtained in one species to a different one. A great deal of lip-service has been paid to knowledge of this sort in this as in other fields.

Roles of the Kidney

Table I shows some of the possible roles of the kidney in hypertension. In attempting to cover this field adequately, I will show great bias in the selection and interpretation of the most significant contributions.

TABLE I.—*Possible Roles of Kidney in Hypertension*

1. Failure to excrete or destroy an extrarenal pressor substance
2. Failure to produce a vasodilator
3. Increased responsiveness of normal pressor mechanisms
4. Decreased response of baroreceptors
5. Stimulation of some extrarenal pressor system—e.g., the adrenal
6. Redistribution of electrolytes and water
7. Production of a vasoconstrictor

Failure of Excretion or Destruction

I previously considered the concept of uraemia as having a causal role in hypertension, and discussed the differences in man between anuria with acute glomerulonephritis and anuria with tubular necrosis in their different effects on the blood-pressure. It was natural for early workers in this field to wonder whether it was possible to reproduce this sort of situation experimentally; for example, Grollman *et al.* (1943) showed that in the rat subjected to complete nephrectomy the blood-pressure would rise and would stay up so long as the animal lived. This did not clarify the situation, however, with respect to the failure of excretion, and Grollman *et al.* (1949) went further with the nephrectomized dog and showed that when the animal was maintained in good condition by dialysis, so that its blood urea was kept down, hypertension still supervened. This showed very clearly that a failure to excrete could not alone be invoked. These experiments have been confirmed by Floyer (1951) in the rat and by Kolff and Page (1955) in the dog.

It was pointed out that with the kidney transplant in the identical twins mentioned in the first lecture (Murray *et al.*, 1958) the blood-pressure subsided after the introduction of the healthy kidney while the diseased ones were still present. This is in direct line with the observations of Muirhead *et al.* (1956), who showed in the dog that a homograft would reduce the blood-pressure of the nephrectomized animal to normal. In our own experience (Robertson and Peart, 1958, unpublished), using the rabbit with a clipped kidney to produce hypertension, a rise in blood urea is the usual concomitant of a rise in blood-pressure. This is shown in Fig. 1, where it can be seen that a high blood-pressure is never present with a blood urea which is within the limits of normal. It can be further seen that there is no direct relation in this preparation between the level of blood urea and the rise of blood-

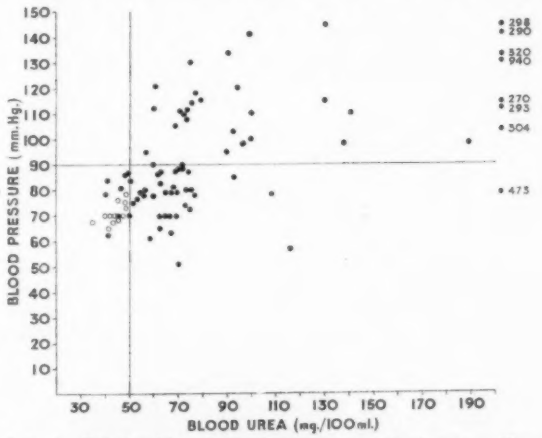

FIG. 1.—Relationship of blood-pressure to blood urea. The graph is constructed from 90 observations on 58 rabbits. ○= normal rabbits which all have a blood urea less than 50 mg./100 ml., represented by the vertical line, and a blood-pressure less than 90 mm. Hg, represented by the horizontal line. No rabbit has a blood-pressure higher than 90 mm. Hg without a rise of blood urea. ●=One kidney removed, the other renal artery constricted.

pressure. In some experimental situations this rise of blood urea, and other things consequent upon it, perhaps may play some part, nevertheless, in the rise of blood-pressure. Surprisingly few complete studies have been made on this aspect of hypertension associated with interference with the kidney, and some impairment of renal function is often produced.

From the sort of observation considered above, there arose the concept that all renal hypertension might be explained by the bringing into play of extrarenal factors, since it was clear that hypertension would develop in the absence of the kidneys. This concept is known as renoprival hypertension. In addition to covering the possibility of failure of excretion, it also includes the

*The second of two Goulstonian Lectures delivered before the Royal College of Physicians of London on January 20 and 22, 1959. The first was published in last week's *Journal*.

possible metabolic effects of the presence of the normal kidney. That extrarenal factors are brought into play in any form of renal hypertension is suggested by the observations of Pickering (1945) in the rabbit, when he showed that removal of the clipped kidney within the first eight weeks was followed by a fall of blood-pressure to normal, but that after eight weeks the blood-pressure would stay up.

Further, in the rabbit, Daniel *et al.* (1954) showed that removing the clip from the renal artery did not relieve the hypertension when this had been present for 12 weeks. This was in contrast to the observations of Blacket and Sellers (1951), who stated that the blood-pressure would fall if this were done. This conflict may depend upon the state of the renal artery after clipping in the two sets of experiments. In the rat, Byrom and Dodson (1949) showed that the blood-pressure would fall when the clip was removed up to the twelfth week, and this could be related to the observations of Wilson and Byrom (1941), who showed that whether the blood-pressure remained up or came down when a clipped kidney was removed depended on whether arterial change had occurred in the opposite kidney. From this arose the concept of the vicious circle in renal hypertension due to unilateral disease. This work was extended by Floyer (1955), and certainly in the rat the perpetuation of hypertension by vascular damage to the opposite kidney seems well established.

The conclusion, then, seems to be that in most forms of renal hypertension a change undoubtedly occurs in the body which leads to maintenance of the hypertension when the damaged kidney is removed. Whatever the mechanism is, it seems to take a certain minimum time to come into operation. In man, however, unilateral renal disease can be in existence for many years and a successful result can still occur with unilateral nephrectomy (Pickering and Heptinstall, 1953), so that the situation must be examined for each particular species and type of hypertension.

The protective action of healthy renal tissue in some situations and, paradoxically, its failure to protect with certain forms of renal hypertension, have been further clarified by the experiment first performed by Rodbard and Katz (1941). In the dog they clamped one renal artery and led the ureter from the opposite normal kidney into the inferior vena cava. Removal of the "ischaemic kidney" then led to a fall in blood-pressure to normal within a few hours, just as if a normal kidney had been present. This suggests that it is some metabolic function of the kidney rather than an excretory function. This type of experiment has been repeated by Grollman *et al.* (1949) in the dog and by Floyer (1955) in the rat with exactly the same result. These observations are clearly the starting-point for further work on this aspect of kidney function in hypertension.

Failure of Vasodilator Production

The hypothesis that the kidney has its main effect on the blood-pressure by providing a vasodilator to keep the blood-pressure down and that hypertension may be due to renal damage, with a failure of production of such a substance or effect was first propounded by Grollman *et al.* (1940). There is no direct evidence showing the production of such a vasodilator. However, Hamilton and Grollman (1958) have shown that a purified extract of kidneys when fed to rats with renal hypertension has the property of lowering the blood-pressure. The exact significance of this observation requires much further work before it can be defined.

Increased Response of a Normal Pressor Mechanism

It would, of course, be possible for a diseased kidney to produce a substance which increased the effects of the normal known pressor systems in the body. For example, the sympathetic nervous system could have an increased effect due to some sort of facilitation, either in the hypothalamus, at the ganglia, or on the effect of noradrenaline liberated at the nerve endings. There is no good evidence which indicates that this is so, whereas there is excellent evidence that the sympathetic nervous system is not playing a causal part in any form of sustained hypertension (Pickering, 1936a). Much has been made of the fact that in animals made hypertensive by renal interference the blood-pressure cannot be lowered readily in the first few weeks by drugs such as yohimbine or pentolinium (Reed *et al.*, 1944 ; Goldblatt, 1958c), but that when the hypertension has been in existence for many weeks these drugs become capable of lowering the blood-pressure, suggesting that a nervous mechanism may be important. This is a very indirect method of assaying nervous activity.

From the point of view of an increased sensitivity to substances like noradrenaline, it must always be remembered that in hypertension the peripheral resistance arterioles must be narrower than normal, and that observations of increased rises of blood-pressure to intravenous injections of pressor substances do not constitute proof of increased sensitivity of blood-vessels, merely that the drug is acting on narrower vessels (Ogden *et al.*, 1940 ; Conway, 1955, 1958 ; Duff, 1957).

Decreased Response of the Baroreceptors

Heymans (1956) has proposed the view that the fault in hypertension may lie in the baroreceptors, such as the carotid sinus, and that they, by altering their response, allow the blood-pressure to rise to a higher level. It has always seemed to me unlikely as a primary cause, and certainly the mechanisms for adjusting the blood-pressure over long periods in the body seem poor, particularly so far as rises of blood-pressure are concerned. It appears that if a minimum blood-flow is maintained to particular tissues, then the level of blood-pressure is of less importance. The most significant observation in this field is that of McCubbin, Green, and Page (1956), who showed in the dog with renal hypertension that the depressor mechanism rapidly became reset at the higher level of blood-pressure obtaining, and only came into play temporarily when the blood-pressure was even further elevated.

Stimulation of Extrarenal Pressor System

Since, as has been seen previously, extrarenal pressor systems must come into play in renal hypertension, the idea that the kidney might stimulate such a system must be considered. The main end-organ in this respect is, of course, the adrenal. This hypothesis received a great fillip when Goldblatt (1937) showed in the dog with renal clamp hypertension that adrenalectomy would return the blood-pressure to normal, and that prior adrenalectomy would prevent the development of such hypertension. These experiments led directly to the performance of adrenalectomy in man for the relief of hypertension. It must be said that this operation has not proved to be very successful in most patients, though there are some in whom a good result has been achieved, and it may be that the operation has too often been performed in the very severe cases (Thorn *et al.*, 1952 ; Jeffers *et al.*, 1953). Experimentally, the most

significant observation, however, is that of Fregly (1957), who showed that in the rat after adrenalectomy it was still possible to cause hypertension by clamping the renal artery. Overall, I believe there is no direct evidence of overactivity of the adrenals in any form of renal hypertension, and that the adrenals merely play a permissive part, maintaining the normal background on which hypertension develops.

Redistribution of Water and Electrolytes

As the kidneys play such an important part in the maintenance of the water and electrolyte balance in the body, it is natural to wonder whether a disturbance in this function could in itself lead to hypertension. It is clear that a mere retention of sodium and of water, as in cardiac failure and cirrhosis of the liver, does not in itself lead to a raised blood-pressure, and the aspect which has received most study is that of an altered distribution between extracellular and intracellular tissues. Eichelberger (1943) was the first to suggest that there might be an increase in intracellular sodium in voluntary muscle in hypertension, and Tobian and Binion (1954) have claimed that in the aorta of man and other animals with renal hypertension there is a definite increase in intracellular sodium. Ledingham (1953) claimed that in the rat with renal hypertension the intracellular sodium in heart muscle was lower than normal. The difficulties that stand in the way of measuring the true intracellular composition of any tissue should be pointed out.

In between the cells lies an undetermined amount of extracellular fluid; it is extremely difficult to make an accurate allowance for changes in this quantity, and this may throw out the determinations and lead to false conclusions. In acute experiments, Friedman *et al.* (1957) have claimed that the normal response of blood-vessels in animals to an acute rise of blood-pressure induced by such substances as noradrenaline and pitressin is for sodium and water to enter and potassium to leave the cell within seconds. Studies in man of the total body sodium, which might, of course, be related to elevation within cells, since extracellular sodium is not raised in most forms of hypertension, do not show any consistent relation to the level of blood-pressure. Ross (1956) found an elevated total exchangeable sodium in some patients, but lowering this by treatment was not related necessarily to lowering the blood-pressure. Moore *et al.* (1954) and Hollander *et al.* (1956–7) have not found an increase in total exchangeable sodium. It is, of course, tempting to wonder whether the entry of sodium and water into intimal or smooth-muscle cells and arterioles could lead to swelling and therefore to an increase in the peripheral resistance, but there is no real evidence bearing on this aspect.

Effect on Kidney Excretion

From the experiments on animals, it has been known for many years that renal hypertension in particular is associated with an increased excretion of both chloride and water (Farnsworth and Barker, 1943). Brodsky and Graubarth (1953) were the first to show that the patient with high blood-pressure behaves differently in response to sodium-loading compared with the normal in that the kidney then excretes much more sodium. Cottier *et al.* (1958) have shown that the patient with hypertension is excreting water and sodium at an increased rate compared with the normal. These observations would lead one to suppose that sodium depletion would be inevitable. However, Sapirstein (1958) has pointed out that, despite the increased total excretion of sodium, there is relatively more water excreted than in the normal kidney, so that the effect would be to increase the body sodium relative to water. It may be asked whether this is a cause of the hypertension or whether the hypertension is the cause of the change in renal function.

White (1950) and Selkurt (1951) showed in the dog that the excretion of sodium and water was directly proportional to the pressure in the renal artery, so that it would be expected that a rise in the pressure would lead to an increase of sodium and water excretion. There is very strong evidence to support the view that these changes in the kidney are secondary to the rise in blood-pressure, since Thompson *et al.* (1954) showed that lowering the blood-pressure by sympathectomy lowered the excretion of sodium and water towards normal, and, similarly, Hollander *et al.* (1956–7) have shown the same effect with hypotensive drugs. The overall view, then, is that, while there is this abnormality in handling sodium and water in hypertension, it is a secondary and not a primary happening.

Vasoconstrictors

The production or occurrence of vasoconstrictors in relation to renal hypertension has a very long history. In 1898 Tigerstedt and Bergman discovered that saline extracts of kidney contained a pressor substance which they named renin. They subsequently showed most of its properties as a protein, but this work then lay fallow, despite interest in the relation between the kidney and high blood-pressure, for thirty-six years until Goldblatt *et al.* (1934) performed their memorable experiment of clamping the renal artery, and showed that this sort of interference with the kidney circulation led to hypertension. Interest was then reawakened in kidney extracts, and among others Pickering and Prinzmetal (1938a) confirmed the existence of renin.

Braun-Menéndez *et al.* (1939) and Page and Helmer (1940) independently arrived at the conclusion that renin must be an enzyme acting on a substrate in the plasma to produce the end-product which received the names of hypertensin and angiotonin. Braun-Menéndez and Page (1958) have suggested the name angiotensin for this final product. Both renin and hypertensin are extremely active in raising the blood-pressure, and Fig. 2 shows this action in the rat. The rounded pressor action of renin, the enzyme-producing hypertensin, during its circulation is to be compared with the short-acting hypertensin effect. It is known that, in the rabbit kidney, renin is situated very close to the glomeruli (Cook *et al.*, 1957; Cook and Pickering, 1958); certainly not in the tubules, but in which precise structure has yet to be determined.

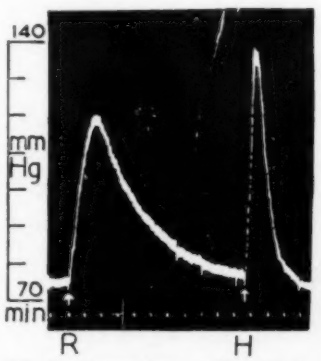

FIG. 2.—Comparison of the pressor action of renin and hypertensin. Rat blood-pressure. R and H = injection of renin and hypertensin respectively. Note the difference in the shape of the pressor responses.

Hypertensin

Hypertensin, or angiotonin, has been isolated and its amino-acid sequence determined (Peart, 1955, 1956; Elliott and Peart, 1956, 1957; Skeggs *et al.*, 1955, 1956b).

1	2	3	4	5	6	7	8	9	10
Asp	Arg	Val	Tyr	Val	His	Pro	Phe	His	Leu
Elliott & Peart Ox substrate									
Asp	Arg	"	" I	Ileu	"	"	"	"	"
Skeggs et al. Horse substrate			↘ II						
Asp	Arg	"	"	Ileu	"	"	"		
Asp	Arg	"	"	Val	"	"	"	"	"
NH_2 *Schwyzer et al. Synthetic*									

FIG. 3.—Structural relationship of natural and synthetic hypertensin peptides. Amino-acid sequences.

Synthesis of this and similar peptides has been achieved by Schwyzer and Sieber (1956), Rittel *et al.* (1957), Bumpus *et al.* (1957), and Schwyzer *et al.* (1958). Fig. 3 shows the relation between these peptides. Skeggs *et al.* (1956a) showed that there was present in normal plasma a "converting enzyme" which was capable of removing the two C terminal amino-acids, his-leu, from the decapeptide and converting it to the octapeptide, which was equally active in raising the blood-pressure. It is therefore believed that it is the octapeptide which normally is the substance active in the circulation. It is also known that these peptides act by directly contracting the smooth muscle of the arterial wall.

With the advance in knowledge of the biochemistry of renin and hypertensin, it has been possible to re-examine the proposition that these substances have a role in human and experimental hypertension. In the past twenty years there have been numerous claims that renin is responsible for a raised blood-pressure in one or other of these situations, and before discussing them I would like to report some of our own unpublished observations.

The first essential in man is to be able to measure renin in the circulation accurately. Robertson and I decided that it was best to allow human renin to make hypertensin and then to assay the latter substance in the rat, since this preparation is extremely sensitive to hypertensin. It should here be pointed out that hypertensin is up to twenty times as active, molecule for molecule, in raising the blood-pressure as is noradrenaline. Fig. 4 shows a typical bracket assay

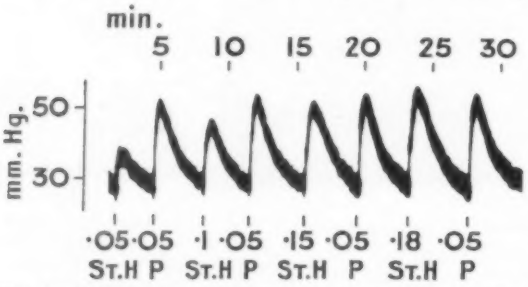

FIG. 4.—Human hypertensin assay. Rat blood-pressure. P = unknown plasma. St.H = standard human hypertensin. Doses in ml. Result: 0.05 P ≡ 0.15–0.18 St.H.

of human hypertensin in the rat. We decided that it was necessary to be able to collect blood from both kidneys in man almost simultaneously, so that, especially in unilateral renal disease, we would then be able to compare the blood from both kidneys. A guided tip catheter was therefore devised (Peart and Sutton, 1958), and samples were collected readily by this means. Fig. 5 shows the catheter. In addition, samples were collected direct from the renal vein at operation in many patients. Table II shows that a wide range of patients with severe hypertension were studied, including those with renal-artery stenosis. The blood collected from the renal veins in this way was incubated, and, as control, renin was added to it to show that in all cases

FIG. 5.—Guided tip catheter. Traction on the nylon thread bends the tip as needed.

TABLE II.—*Samples of Renal-vein Blood in Hypertension*

No. of Patients	*Diagnosis*
14	"Essential" hypertension (8 malignant)
3	Pyelonephritis (1 malignant)
2	Glomerulonephritis (1 malignant)
1	Polycystic kidney
2	Unilateral hydronephrosis
3	Stenosed renal artery
1	Coarctation of aorta

the possibility of making hypertensin with the blood collected was present. Fig. 6 shows a typical assay in a patient with severe renal hypertension.

In all these investigations it was not possible to demonstrate any renin in the renal-vein blood. The amount of hypertensin which it was possible to make from the blood of normal and hypertensive patients was considerable — over 1 μg. per ml. of plasma. Fig. 7 compares the amounts of hypertensin made by adding renin to plasma from a normal and a hypertensive patient to emphasize this point further. Both these subjects fell within the same range of production of hypertensin, and the lower limits of the assay at which we were usually working are shown in the bottom left-hand rectangle in Fig. 7. Now this evidence is in direct conflict with reports that renin is sometimes found in renal-vein blood in man (Dexter and Haynes, 1944; Haynes *et al.*, 1947; Margolin *et al.*, 1957). I believe that before any worker claims that renin or hypertensin is present in blood the criteria in Table III should be adhered to. There have been so many claims that have only added to confusion because of lack of rigid proof, and at this stage these criteria are essential to clarify the situation. It is so easy to produce artifacts in blood, and these vary according to the type of assay used.

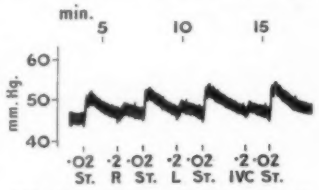

FIG. 6.—Assay of human plasma in the rat. St. = standard human hypertensin. R = right kidney. L = left kidney. IVC = inferior vena cava. Doses in ml. No detectable hypertensin in any sample.

One objection to the experiments described above is that the assay might be too insensitive for the amounts of renin and hypertensin responsible for the hypertension in the patients studied. From the experiments we have performed, using synthetic hypertensin (Pickering, Sanderson, and Peart, 1958, unpublished), we know that it requires about 5–10 μg. per minute intravenously to produce distinct hypertension in man. If we assume

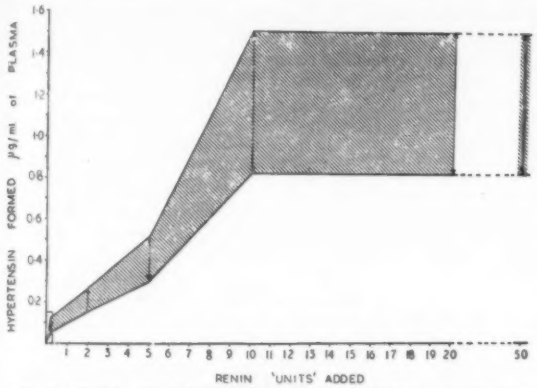

FIG. 7.—Renin assay in human plasma. Abscissa: amount of standard renin added to same volume of plasma. Ordinate: hypertensin concentration (Asp-NH_2 Val 5). Small rectangle at bottom left is usual working range. Area of curve represents bracket limits of assay. Curve constructed by assay on normal peripheral plasma and on renal-vein plasma from patient with severe renal hypertension.

from renal plasma flow, as derived from para-aminohippurate (P.A.H.) clearance techniques, that this amount would be added to 250 ml. of plasma per minute, then we obtain a concentration of 0.02–0.04 µg. per ml. of plasma, which is within our assay range on the rat. Further, most of our patients studied had severe hypertension and the renal plasma flow was much lower than this, so that we think we should have been able to demonstrate hypertensin if it had been produced there by renin.

It might be argued that in patients with hypertension there could be a greater response to smaller quantities of hypertensin than those required in the normal, or that some other mechanism is responsible for maintaining the blood-pressure in the presence of smaller quantities of hypertensin which could be regarded as the initiating cause. This secondary mechanism has been discussed previously. It has further been claimed that if the renal artery in man and animals is clamped to produce total ischaemia for minutes, the venous blood contains renin on releasing the clamp (Quinby *et al.*, 1945). We have repeated these experiments in patients whose renal arteries had to be clamped during the course of an operation, and we have been unable to show the presence of renin, though it was easy to demonstrate renin added to the blood.

TABLE III.—*Suggested Criteria for Identification of Renin and Hypertensin*

Renin

1. The form of the pressor effect should be identical with standard renin
2. Activity should be lost by heating
3. The ability to make hypertensin should be demonstrated

Hypertensin

1. The form of the pressor effect should be identical with pure substance
2a. Action on other test objects should be the same as the pure substance
2b. Identity of behaviour with the pure substance using different methods of physical separation

Renin in Renal-artery Clipping

Following the renal-artery-clamp procedure of Goldblatt *et al.* (1934), it became a natural assumption that the hypertension thereby caused was due to the release of renin into the circulation, but direct evidence is striking by its absence. Robertson and I (1958, unpublished) have re-examined this problem in the rabbit. Rabbit renin can be assayed directly and readily in the rat. Rabbits were made hypertensive by putting a clip on the renal artery and removing the other kidney (Pickering and Prinzmetal, 1938b). Samples were collected from the renal vein of rabbits at all stages of hypertension, both early (up to one week) and late (two to three months), and with both mild and severe hypertension. In some instances samples were collected from the anaesthetized animals. In others a catheter was inserted into the renal vein via the external jugular vein, under ether, and samples were subsequently collected from the conscious animal.

In order to see whether we could detect renin infused into the rabbits so that their blood-pressure was raised to the same level as in renal-artery clamping, we performed another type of experiment. A catheter was introduced just within the mouth of the renal vein and a fine nylon catheter pushed through it right up to the kidney. Infusion of renin was made through this and the blood-pressure raised (Fig. 8). At no time in any rabbit with hypertension due to renal-artery clipping has it been possible to show the presence of renin, yet it has always been possible to demonstrate this substance when infusions were given in the way described, and blood was collected from the mouth of the renal vein. Fig. 9 shows a typical comparative experiment, and relevance is added when it is realized that the infusion experiments were done in animals treated in exactly the same way as those which did develop hypertension but in which, probably due to a too large clip, hypertension did not develop.

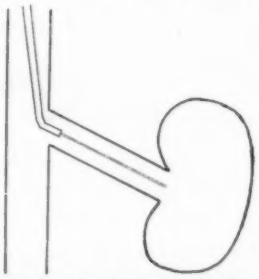

FIG. 8.—Method for infusion of renin into the renal vein with collection of renal-vein blood mixed with renin. Renin infused through the fine catheter. Blood collected through the wider outer catheter.

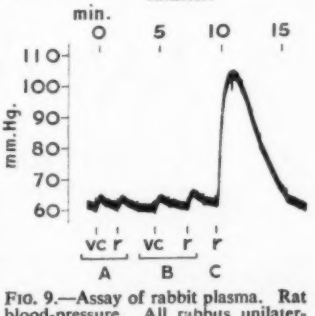

FIG. 9.—Assay of rabbit plasma. Rat blood-pressure. All rabbits unilaterally nephrectomized with renal artery clamp on remaining kidney.

Samples { vc = inferior vena cava below renal veins. r = renal vein.

Animals { A = B.P. 32 mm. above baseline. B = B.P. 52 mm. above baseline. C = no rise of blood-pressure until renin infused into end of renal vein to give 30 mm. rise of blood-pressure. Sample taken from mouth of vein. Dose 0.1 ml.

Again, it may be asked how it is that these negative findings were obtained when others have claimed the presence of renin in this sort of hypertension. The direct demonstration, I think, is the only one worth while, since all the other errors which may creep into the interpretation of indirect methods are avoided. In performing a direct investigation, the presence of artifacts has to be rigorously excluded, and in handling blood which has to be assayed elsewhere artifacts

readily creep in. Fig. 10 shows a typical artifact produced in human blood obtained from the renal vein, which has a long action like that of renin. Fig. 11 shows an artifact which is produced by incubating rabbit plasma and which is indistinguishable from hypertensin in its effects on the blood-pressure. Some reports of renin and hypertensin may be based on this sort of finding.

Tachyphylaxis

If successive doses of renin are given to certain animals the response dies away. This is especially so in the rabbit, and Taggart and Drury (1940) made use of this to determine the role of renin in the renal-clip hypertension. They injected renin into such hypertensive animals until the response was abolished, yet the animals remained hypertensive, suggesting that they could not be producing renin themselves to maintain the hypertension. Goldblatt (1958b) has claimed that he has never seen tachyphylaxis in the dog, but it certainly occurs in the rabbit, even with purified preparations of renin, and Fig. 12 shows a typical effect.

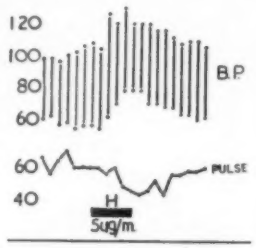

FIG. 13.—Effect on blood-pressure and pulse in man of an infusion of Asp-NH, ileu 5 octapeptide (H=5 μg./min.).

Antirenin

Johnson and Wakerlin (1940) conceived the idea that, if it were possible to make an antibody to renin, injections of it into animals with renal hypertension and observation of the subsequent effects on blood-pressure would define the role of renin. They, and subsequently Goldblatt *et al.* (1951), have shown that such antirenin sera are capable of lowering the blood-pressure of the dog with renal-artery-clamp hypertension. There is no doubt about the observations, but I am far from convinced that this proves that the effect is due to the antirenin contained in the sera. These sera are not pure substances, and this indirect approach will require the use of pure renin to produce the antibodies before more credence can be given to this type of experiment.

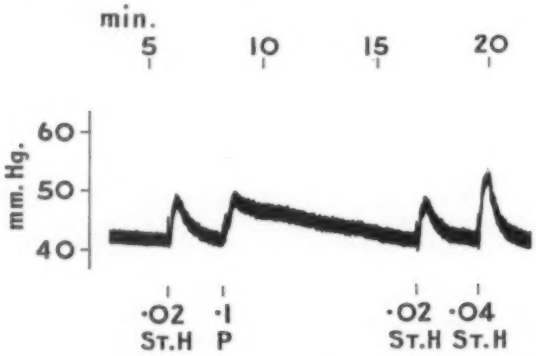

FIG. 10.—Long-acting pressor artifact in human plasma. Rat blood-pressure. P=plasma. St.H=standard human hypertensin. Doses in ml.

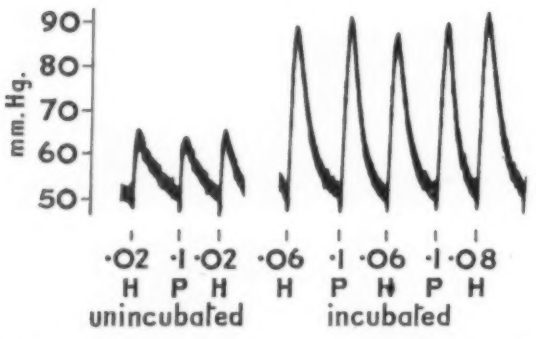

FIG. 11.—The appearance of a hypertensin-like artifact in rabbit plasma on incubation at 37° C. for 20 minutes. H=standard. P=plasma. Doses in ml. The small effect before incubation is quite common.

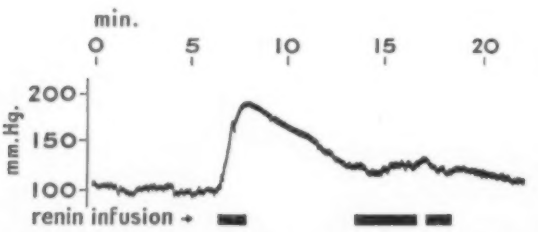

FIG. 12.—Renin tachyphylaxis in the rabbit. The dark blocks represent infusions of renin given at a steady rate during the period indicated. It can be seen that after the first response there is no further response.

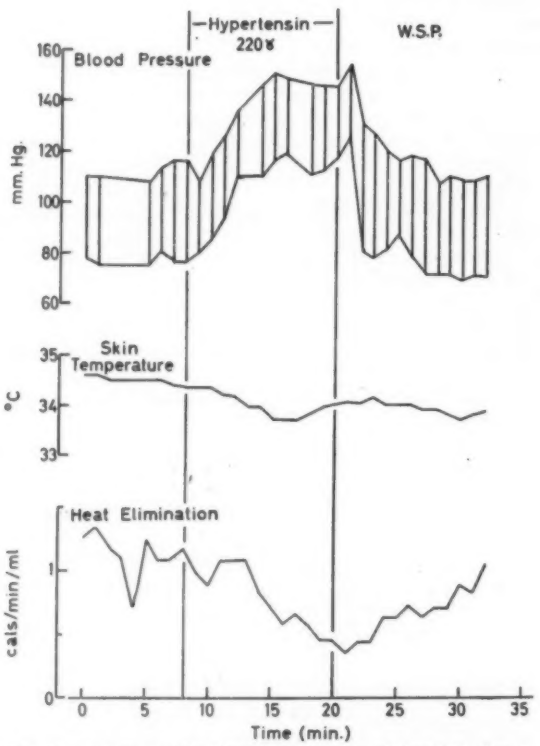

FIG. 14.—Effect on skin blood-flow in man of Asp-NH, ileu 5 octapeptide, measured by thermocouple and hand calorimetry. The bottom two sections show the fall in heat output and skin temperature during the infusion.

Actions of Hypertensin

Knowledge of the actions in man of pure hypertensin may be expected to throw light on its possible role in hypertension. Sanderson, Pickering, and I (1958, unpublished), Bock and Krecke (1958), and Bock *et al.* (1958a, 1958b) have investigated these actions. Fig. 13 shows the typical effect on blood-pressure and pulse. As with noradrenaline, the pulse is slowed with rise of blood-pressure. With moderate rises of blood-pressure the subject is not aware of any unpleasant sensations, but with higher rises peculiar mental effects enter, difficult to define.

Skin Blood-flow

Intravenous infusions of hypertensin lower the skin blood flow as the blood-pressure rises. This is shown in Fig. 14. As the hand blood-flow is within normal limits in most forms of hypertension this suggests immediately that if hypertension is playing a part considerable readjustment would have to take place in the circulation.

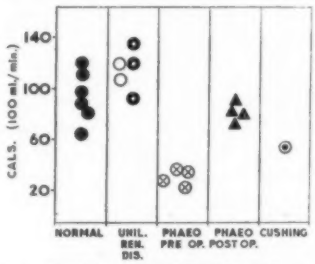

FIG. 15.—Hand blood-flow in various forms of hypertension measured by calorimetry with body-heating to eliminate sympathetic tone (so-called maximal heat elimination). Shown are normals, unilateral renal disease (open circle represents renal-artery stenosis), phaeochromocytoma before and after tumour removal, Cushing's syndrome.

Hand Blood-flow in Hypertension

In view of the observations made and the effects of pure hypertensin in reducing the hand blood-flow in normal subjects, Dr. J. J. Brown has reinvestigated the hand blood-flow in various forms of hypertension. This has especial relevance in that if one considers the state of the circulation in a patient with phaeochromocytoma where noradrenaline and adrenaline are circulating, the hand and skin blood-flow are found to be reduced, since these substances have special vasoconstrictor effects in the skin (Barnett *et al.*, 1950; Hamilton *et al.*, 1953). It has been commented that hypertensin infusions led to a fall in skin blood-flow, and therefore we wondered whether we would find a reduced hand blood-flow in patients with renal hypertension, especially renal-artery stenosis.

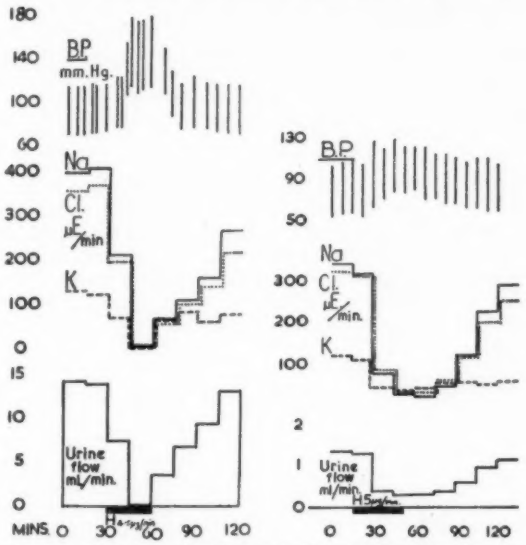

FIG. 17.—Effect on urine flow and electrolyte excretion in man of infusion of Asp-NH_2 val 5 octapeptide (H). Left: High flow; H=4.5 μg./min. Right: Low flow; H=5 μg./min. The flow rate and electrolyte excretion are both greatly reduced.

Fig. 15 compares the hand blood-flow in various forms of hypertension. The low flow in the patients with phaeochromocytoma is noted and is contrasted with the normal flow existing in patients with renal hypertension, including renal-artery stenosis. In acute nephritis, Pickering (1936b) has previously found that the hand blood-flow was raised or had a high normal value, and that with decline in the blood-pressure the blood-flow also dropped. Readjustment of the circulation to noradrenaline does not seem to prevent the demonstration of its effects, whereas if hypertensin is responsible for the hypertension in patients with renal disease, it is perhaps surprising that their hand blood-flow is still within high normal limits. These arguments, however,

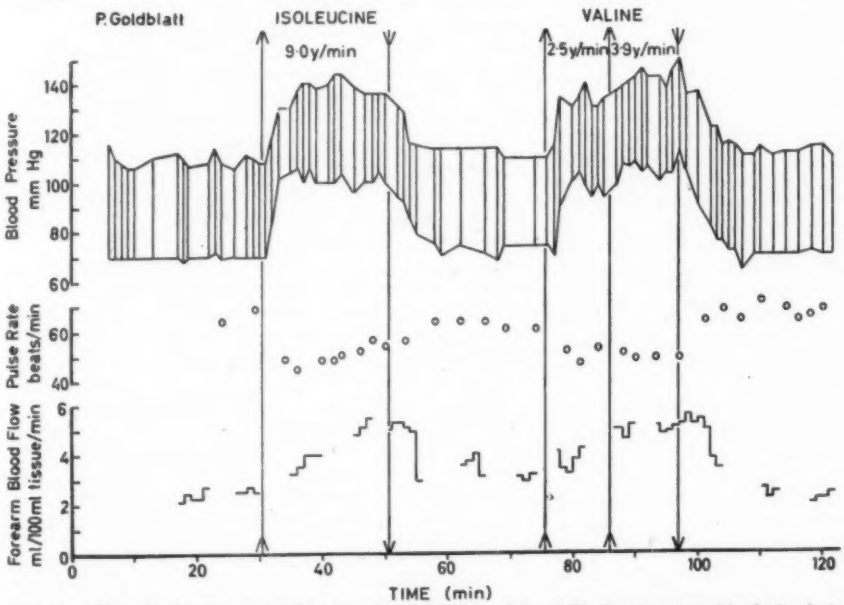

FIG. 16.—Effect on forearm blood-flow in man of infusion of Asp-NH_2 ileu 5 octapeptide (isoleucine) and Asp-NH_2 val 5 octapeptide (valine). The rise during both periods of infusion is shown.

are indirect, and I place much more emphasis on the direct methods described previously.

Forearm and Muscle

As the blood-pressure rises with infusions the forearm blood-flow also rises, and Fig. 16 shows the typical effects of infusion of two types of hypertensin. Bock *et al.* (1958b) have shown by direct measurement of muscle blood-flow that this rises. This is consistent with the findings on forearm blood-flow, which is a mixture of skin and muscle flow. Hypertensin is therefore not a very potent constrictor of muscle vessels.

Effects on Kidneys

Of extreme interest are the effects on the kidney, since, as was discussed above, there are changes in hypertension leading to an increased output of water and sodium. In the normal subject the consistent effect is greatly to reduce urine flow and electrolyte excretion. This occurs with only moderate rises of blood-pressure, and with larger rises in blood-pressure it is possible almost to stop urine flow. This effect is shown in Fig. 17, and occurs at high and low rates of urine flow. That it is a direct effect and not one mediated through antidiuretic hormone is suggested by the experiment we performed in a patient with diabetes insipidus (Dr. de Wardener, St. Thomas's Hospital), where the effect was shown to be the same as in the normal subject. In addition, we have noted a fall in inulin and P.A.H. clearances, pointing to a vasoconstriction in the renal arteries (Fig. 18). These effects, of course, are not like anything seen in any form of hypertension, except perhaps acute glomerulonephritis, but it must be remembered that acute experiments do not necessarily give valid information about chronic states in man, and Dr. J. J. Brown (1959, unpublished) has repeated these observations in patients with severe renal hypertension and discovered that in many, with infusions of small amounts of hypertensin, sufficient to slightly raise their blood-pressure, the urine flow and electrolyte excretion rise in contrast to the normal (Fig. 19).

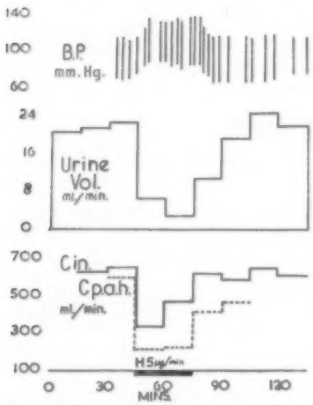

FIG. 18.—Effect in man on inulin clearance (C in.) and P.A.H. clearance (C p.a.h.) of infusion of Asp-NH, val 5 octapeptide (H) 5 µg./min. Both are reduced, as is the urine flow.

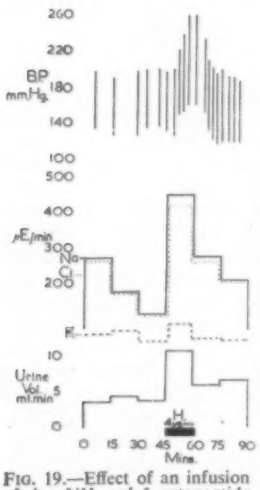

FIG. 19.—Effect of an infusion of Asp-NH, val 5 octapeptide (H) 4 µg./min. on the urine flow and electrolyte excretion in a patient with severe renal hypertension. Both factors rise in contrast with the normal subject.

It is difficult to believe that in these patients the hypertensin that was infused was being added to endogenous hypertensin responsible for the high blood-pressure and the existing normal renal excretion of water and electrolytes.

The circulatory effects thus seem to be that pure hypertensin is vasoconstrictor in most areas where it has been studied and that the findings do not fall into line with anything that is known of renal hypertension, except perhaps the effects on the kidney in acute nephritis. These findings must be contrasted with the claims of Kahn *et al.* (1952) in patients with malignant hypertension where the blood was said to contain up to twenty times as much hypertensin as normal, and with the similar claims of Gollan *et al.* (1948) and of Skeggs *et al.* (1951) in dogs with renal-artery-clamp hypertension, where hypertensin was similarly incriminated as the cause of the raised blood-pressure. Immediately one must say that there is a discrepancy here which requires explanation. One cannot transfer arguments from dog to man, but the onus of proof of a high order seems to me to be fairly placed on those making the claim, and I do not think that the evidence of the presence of hypertensin is sufficient. The demonstration of a pressor action in an extract should be backed up by other methods—for example, parallel pharmacological assay or physical separation—so that we may at last bring clarity.

Summary and Conclusions

An examination of the morbid anatomical and histological changes in the kidney in hypertension shows no consistent relation to the level of blood-pressure. In man the often-found ischaemic change in the tubules is not uniform and is by no means paralleled in the experimental situation.

That arterial obstruction to one kidney may lead to hypertension in man, as well as in the animal with a Goldblatt kidney, has been well established by the demonstration that reconstruction of the stenosed artery or removal of the kidney beyond may return the blood-pressure to normal. The diagnostic criteria and investigation of function of the kidney in this condition are discussed and emphasis is laid upon the necessity for proper investigation before over-enthusiastic surgery is performed on arteriographic appearances.

Some possible roles of the kidney in hypertension are considered critically, and an attempt is made to distinguish those changes which occur as a consequence of the high blood-pressure as opposed to those which may have a causal role.

Special emphasis is given to a consideration of the role of vasoconstrictors emerging from the kidney and an assessment of the renin–hypertensin system made. Investigations and experiments performed in man and in the rabbit are described, which lead to the conclusion that renin cannot be wholly, if at all, responsible for the type of hypertension studied, which included clinical and experimental examples of renal-artery obstruction. The use of pure synthetic hypertensin peptide in human investigation is described and the qualitative and quantitative considerations which argue against its role in hypertension of the sort studied are considered.

Thanks are due to my colleagues at St. Mary's Hospital for their co-operation, and especially to Dr. D. Sutton for the arteriograms, to Dr. Victor Wynn for data on the patients with anuria, to Dr. R. H. Heptinstall for Special Plate Fig. 1, Lecture I and for reports on the renal histology,

and to Mr. K. Owen for the operative findings. Many members of my medical unit collaborated in this work, and I am especially indebted to Dr. J. J. Brown, Dr. J. I. S. Robertson, Dr. N. Stone, Mr. F. Diggins, and Mrs. N. Mendelsson.

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MIGRAINE AND ITS RELATIONSHIP TO HYPERTENSION*

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Headaches present a common and important group of symptoms in general practice, the accurate diagnosis and treatment of which may be the despair of the practitioner. Until comparatively recently the problem of headache received only scant attention and the mechanisms producing the various types of headaches were poorly understood. The importance of the problem is aptly expressed in the following words: "If one should search for a human ill which has manifested itself most widely during all times and among all people, there can be little doubt headache would achieve this undesirable distinction" (A. H. Riley, cited by Meuller, 1951).

This study was an attempt to give some indication of the incidence in general practice of one common and distressing variety of headache—namely, migraine—and, secondly, to establish a possible relationship between migraine and the later development of hypertension.

Though the condition has been recognized for many centuries it was not until the beginning of the second world war that any real progress was made towards solving the mystery of this distressing complaint. Migraine can scarcely be called a serious condition, but it is nevertheless an incapacitating one; the unfortunate sufferer may lose a considerable number of working days during a year, while the young mother may be quite incapable of performing her normal household duties for several days following an attack. The problem thus assumes an economic importance which presents an additional challenge to the doctor in his management of the many cases which are bound to come his way in normal day-to-day practice.

The material for this study has been drawn from a population of approximately 6,000 comprising the patients of a practice situated on the outskirts of the City of Liverpool, and the observations were made over a period of three years, 1954 to 1957.

Approach to the Problem

The method of approach was as follows. The medical record of every patient in the practice was examined and any reference to migraine or recurrent headaches suggestive of migraine was recorded along with the patient's name, age, and address. A total of 5,785 such records were studied. At the same time, any reference to raised blood-pressure was recorded. These patients were then interviewed, and a detailed history taken, followed by physical examination.

The criteria which had to be satisfied before a diagnosis of migraine was made were based on the definition of von Storch (quoted by Marshall, 1949), who listed the following components in order of diagnostic importance: (1) recurrent headache; (2) associated visual symptoms; (3) temporary gastro-intestinal phenomena, usually nausea or vomiting; and (4) a family history of migraine, occasionally an epileptic history.

*The 1959 prize-winning essay for the Charles Oliver Hawthorne Prize awarded by the British Medical Association.

The first of these components associated with one other was necessary before the diagnosis was considered. According to Marshall the diagnosis could be expressed in order of certainty as follows: (1, 2, 3, 4); (1, 2, 4); (1, 3, 4); (1, 2); (1, 3). It will be noted that von Storch does not stress the unilateral nature of the migraine headache. In this study I have insisted on this feature being present, at least at some stage in the history.

To satisfy a diagnosis of hypertension, a diastolic pressure of not less than 100 mm. Hg was chosen as the basic level (Peel, 1950).

Only cases of hypertension labelled "essential" have been included in the study. In most patients the final reading chosen was the average of several readings taken over a period of at least six months, and in many cases over a period of several years. The patients interviewed were questioned regarding their general health, including past medical history. At the conclusion of the history specific questions were asked regarding the nature of any headache, the questions being based on the criteria already stated. Many patients interviewed already knew they suffered from migraine and were in the habit of attending the surgery at regular intervals for treatment. Likewise, many patients were already aware that their blood-pressure was raised and were accustomed to having it recorded periodically (though during the examination the words "high blood-pressure" were carefully avoided).

Findings

A past or present history of migraine was obtained in 281 patients, giving an incidence of 4.85%. Of these, 221 (78.6%) were female and 60 male. Of these 281 patients, 154 (54.8%) gave a family history of migraine. Likewise, examination of 5,785 medical records revealed 161 cases that satisfied the criteria of hypertension previously stated. Of these 161 cases, 128 (80%) were female and 33 (20%) male. Investigation of these patients revealed that 84 (52%) had a past or present history of migraine. Certain points of criticism are, however, at once apparent, and it would seem appropriate to draw attention to these before proceeding further. The most obvious question concerns the accuracy of these records in giving a true indication of the incidence of migraine and hypertension. Obviously, the records would only reveal those patients who had chosen to complain of their disability, or where the condition was diagnosed by chance. Medical records ignore patients whose attacks of migraine are perhaps so infrequent or of such short duration or so mild that they do not consult a doctor.

Accurate figures relating to the incidence of migraine are difficult to obtain. Grimes (1931), in a survey of 15,000 patients in general practice in America, estimated the incidence as 8%. More recently, in a review of migraine, the incidence is quoted as 10% of the population (*J. Amer. med. Ass.*, 1955). Fry (1955–6), in his practice of 5,000 patients, has recorded 145 cases over a period of five years, giving an incidence of 3.5%. The finding that 281 (4.85%) patients satisfied the criteria of migraine compared favourably with that of Fry and also with the incidence reported by Lennox (1941) and Leyton (1954). With regard to the estimate of Grimes it is possible that, with the more accurate and detailed methods of investigation which are now employed, many of his cases might be found to have a definite pathological basis for their headaches. American workers—for example, von Storch—do not

appear to stress the hemicranial nature of migraine and tend to accept as their definition a history of recurrent headaches with either scotomata or gastro-intestinal disturbance or both. This definition would probably tend to allow of a somewhat higher incidence than if the unilateral feature were insisted on in the diagnosis. Confusion between migraine and psychogenic headache is possible, though as a rule the latter is of longer duration and there is no aura.

The finding that 84 (52%) of the 161 patients with hypertension gave a past or present history of migraine would appear almost incredibly high, and the impression was gained that if this proportion were a true one the association between migraine and hypertension would almost certainly have been more widely reported on and more definite conclusions on the subject would already have been reached. Obviously, in this instance the medical records were giving an erroneous impression. Patients complaining of headache are more likely to have their blood-pressure recorded than are patients with other complaints. The symptomless hypertensive is under-represented in such medical records.

It was therefore decided to carry out an analysis of 150 cases of migraine in patients over the age of 30 and to compare them with 150 controls of the same age and sex distribution chosen at random, who gave no history in any way suggestive of migraine. In this way it would be possible to determine whether patients with migraine had blood-pressure above the average for the population. In both groups of patients the following data were recorded: sex, age, and blood-pressure. In the group of patients with migraine the following additional data were recorded: age at onset and severity. The fact that blood-pressure can be influenced by certain well-recognized conditions—for example, renal disorders, endocrine disorders, pregnancy, etc.—has been borne in mind and any doubtful cases have been excluded from the study.

Presentation of Data

Analysis of 150 Cases of Migraine (Aged 30 and Over)

Sex Distribution.—Males 38, females 112. The ratio of females to males of 3 to 1 is influenced by several factors: (*a*) It is generally recognized that females are more free to consult a doctor, especially at surgeries. This trend is revealed in Table I, which shows the total attendance at morning and evening surgeries at the practice concerned in this investigation during a typical four-weeks period in winter. (*b*) The frequent association between migraine and menstruation, which, in view of its regularity, will almost certainly sooner or later send the patient to seek medical advice. (*c*) The conclusion that more women consult a doctor because their headaches are frequently more severe, of longer duration, and are more often accompanied by nausea and vomiting (Lennox, 1941).

TABLE I.—*Relationship Between Sex Incidence of Migraine and Total Attendance at Surgery During a Four-weeks Period*

	Total Attendances	History of Migraine	Test of Significance
Female ..	1,094	112	χ^2 = 8·87 n = 1 P = 0·01
Male ..	703	38	

Age Distribution (Table II).—The age distribution is very similar in males and females, with a decreasing incidence towards the middle age. It is generally recognized that migraine tends to disappear in middle age. In women this decline often follows the menopause (Lennox, 1941), but in others the menopause coincides with an intensification of the headaches (Roberts, 1955).

TABLE II.—*Age Distribution*

Age	Males	Females
30–39	17	43
40–49	9	37
50–59	9	24
60+	3	8
Mean age	44·2 years	44·2 years

Age at Onset (Table III).—Migraine may develop at any age, but the onset is usually in childhood or adolescence, with a tendency to become less frequent with age (Friedman, 1951). In childhood recurrent attacks of vomiting without headache may precede the fully developed migraine attack. However, no age group is exempt, and migraine may not appear until past middle age (Leyton, 1954). That author maintains that migraine which begins late in life tends to increase in frequency and severity rather than decrease with advancing age. The finding of a mean age of onset of 27.9 years for males and 24.5 years for females could in some measure be due to the fact that all these patients were 30 years or older and therefore their memories for age at onset might be less sharp than in younger patients.

TABLE III.—*Age at Onset*

Age	Males	Females
10–19	9	39
20–29	13	46
30–39	10	16
40–49	6	10
50–59	—	1
Mean age at onset ..	27·9 years	24·5 years

Severity of Attacks (Table IV).—The one female in category 1 is probably an underestimate, since patients with such infrequent attacks would be less likely to complain of their headaches. The majority of patients fall into categories 2 and 3. Table V reveals a tendency towards greater severity and higher blood-pressure as the duration of the migraine increases. A possible explanation which might influence the data is that, apart from any relationship between migraine and

TABLE IV.—*Severity of Attacks*

Severity	Males	Females
Category 1	—	1
,, 2	17	27
,, 3	16	78
,, 4	4	6
Mean	2·6	2·8

1 = Attacks less than once every 6 months. 2 = Attacks more frequent than once every 6 months. 3 = Attacks more frequent than once a month. 4 = Attacks more frequent than once a week.

TABLE V.—*Relationship Between Severity, Duration of Migraine, and Level of Blood-pressure in 80 Females Aged 30 to 49*

Duration of Migraine	Average Severity	Average Diastolic B.P.
0–5 years	2·7	81·0
6–9 ,, ...	2·4	82·1
10–14 ,, ...	2·7	86·9
15–19 ,, ...	2·9	80·0
20–24 ,, ...	2·8	80·3
25–29 ,, ...	3·0	90·0
30 and over	3·0	90·0

blood-pressure, the higher levels of blood-pressure could be the effect of age. The average severity among this group is 2.8—that is, roughly one attack a month.

Comparison Between Blood-pressures of 150 Migraine Patients and Blood-pressures of 150 Controls Matched for Age and Sex

Significance.—Age for age, the difference between the mean systolic pressures (Table VI) and between the mean diastolic pressures (Table VII) of the migraine and non-migraine groups is around 10 mm. To simplify calculation, tests of significance were applied to pooled data (Table VIII). As the observed difference between the systolic means is five times the standard error it is highly significant. Since the observed difference between the diastolic means is six times the standard error the result is highly significant. Thus there appears to be a significant difference between the blood-pressure levels of migraine and non-migraine patients.

TABLE VI.—*Systolic Blood-pressures of Male and Female*

Systolic Blood Pressure (mm. Hg)	Patients Aged 30–49		Patients Aged 50+	
	Migraine	Controls	Migraine	Controls
110–	1	7	1	1
120–	26	34	1	2
130–	31	38	3	1
140–	24	16	8	30
150–	7	4	5	12
160–	8	0	8	3
170–	5	0	8	2
180–	2	0	4	0
190–	1	0	4	0
200–	1	—	2	0
Totals ..	106	99	44	51
Mean ..	138·87 mm.	129·1 mm.	159·77 mm.	144·41 mm.

TABLE VII.—*Diastolic Blood-pressure of Male and Female Patients*

Diastolic Blood Pressure (mm. Hg)	Patients Aged 30–49		Patients Aged 50+	
	Migraine	Controls	Migraine	Controls
60–	6	11	0	0
70–	24	42	2	4
80–	39	38	11	18
90–	23	8	4	29
100–	8	0	18	0
110–	4	0	9	0
120–	2	0	0	0
Totals ..	106	99	44	51
Mean ..	84·11 mm.	76·37 mm.	95·68 mm.	85·98 mm.

TABLE VIII.—*Results of Tests of Significance*

Patients	Systolic		Diastolic	
	Mean	S.D.	Mean	S.D.
150 migraine ..	144·86	20·47	87·5	12·69
150 controls ..	134·26	12·06	79·63	8·36
S.E. of diff. ..	±1·94		±1·25	

Relationship of Migraine to Hypertension

In order to study further this aspect of the problem it is essential to know the incidence of migraine in the general population and in those with hypertension. It was decided to estimate this in 300 patients over the age of 40, on the assumption that essential hypertension is uncommon below that age. The 300 patients were seen consecutively as they consulted me at the surgery or during a visit to their homes, the selection being left to chance.

The following information was noted: age, B.P., and history of migraine. In the analysis males and females are combined, and, since hypertension is usually found in older patients, two age-groups were examined: (*a*) 40–49; (*b*) 50 and over.

The χ^2 test was applied, and the results are presented in Table IX.

In the age-group 40 to 49 the level of significance is below the conventional 5%. The trend is in the right direction, but the numbers are probably not large enough to be statistically significant.

In the age-group 50 and over the results of the analysis are highly significant, indicating that the association between migraine and essential hypertension is a real one. The incidence of migraine rises as the blood-pressure increases.

Comment

The possibility of a relationship between migraine and hypertension has been recognized for many years, but the problem has, on the whole, received little attention, and the nature of the relationship remains uncertain and ill-understood.

TABLE IX.—*Relationship of Migraine to Hypertension in 300 Patients*

Systolic					Diastolic				
B.P.	No. of People	No. with History of Migraine	Incidence of Migraine	Test of Significance	B.P.	No. of People	No. with History of Migraine	Incidence of Migraine	Test of Significance
Patients Aged 40–49									
110–	2	0	0/32 = 0%	χ^2 = 4·61 n = 2 P = 0·10	70–	48	0	0/48 = 0%	χ^2 = 4·0 n = 2 P = 0·15
120–	30	0			80–	50	4	4/50 = 8%	
130–	40	1	1/40 = 2·5%		90–	15	1	1/15 = 6·7%	
140–	34	3	4/41 = 9·8%						
150–	7	1							
Total	113	5	5/113 = 4·4%	Not significant	Total	113	5	5/113 = 4·4%	Not significant
Patients Aged 50 and Over									
120–	6	1	2/82 = 2·4%	χ^2 = 29·38 n = 2 P < 0·001	70–	21	1	1/66 = 1·5%	χ^2 = 26·2 n = 2 P < 0·001
130–	24	0			80–	45	0		
140–	52	1			90–	73	10	19/94 = 20·2%	
150–	45	9	16/73 = 20·6%		100–	21	9		
160–	26	6			110–	20	8	12/27 = 44·4%	
170–	2	1			120–	6	3		
180–	13	5	14/32 = 43·8%		130	1	1		
190–	4	2							
200–	15	7							
Total	187	32	32/187 = 17·1%	Significant	Total	187	32	32/187 = 17·1%	Significant

In his monograph on hypertension Janeway (1913) called attention to the not infrequent occurrence of migraine headaches during early life in persons who later had hypertension and "hypertensive headaches." He described the headache as: "One which appears on awakening or wakes the patient in the early morning hours, has its greatest intensity before arising, and passes away either immediately after breakfast, or during the course of the morning, to reappear in the same manner day after day for considerable periods. The intensity of the pain and its location have varied somewhat, the most severe being similar to bad migraine, and in a few cases it is attended by nausea and vomiting." Gardner *et al.* (1940) found that four-fifths of 100 hypertensive patients gave a history of past or present attacks of migraine, contrasted with 15% in the control group. Of the total registrations at the Mayo Clinic, migraine was five times as frequent in hypertensive patients as in those in whom hypertension was not recorded. Atkins (1955) reported that 6 out of 24 patients with migraine had significant hypertension as judged by a mean resting diastolic pressure of over 100 mm. Hg. Of these, four were over 50 years of age, while the youngest was 39. Among 26 control cases only two had significant hypertension.

Until a definite cause for essential hypertension has been established any opinion regarding a possible relationship to migraine must remain nothing more than supposition. Certain facts are, however, already recognized which lend support to a possible association between the two conditions.

1. A family history is common in both conditions. "Studies of the family histories of patients with hypertension have shown a hereditary factor in 76 to 80% of cases" and that "evidence is compatible with the hypothesis that essential hypertension is a hereditary disease conveyed as a Mendelian dominant with a rate of expression of more than 90%" (Platt, 1947).

2. The personality structure of the two disorders has several points in common. Both conditions present evidence of suppressed emotional conflict. According to Ayman (1948) the early symptoms of hypertension are frequently those of psychoneurosis. Emotional stress often seems to precede the onset of hypertension, and anxiety bears a close relationship to the aggravation of existing symptoms in hypertension. Weiss *et al.* (1950) discussed the importance of emotional factors in hypertension and stressed the resemblance to migraine. They believed there was an intimate relationship between the personality structure of the two disorders.

3. Essentially the same mechanism is operative in producing the headache associated with hypertension as in the migraine headache—namely, dilatation and distension of the cranial arteries (Sutherland and Wolff, 1940; Schumacher and Wolff, 1941), though it must be admitted, however, that headache is an unpredictable factor in hypertension.

Any association between migraine and hypertension may be pure chance, since both are common conditions. A patient complaining of recurrent headaches is more likely to have his blood-pressure recorded, and therefore hypertension is more likely to be discovered. The term "essential hypertension" can be used correctly only after known causes of hypertension have been excluded. It is possible, even in the light of our present knowledge, that we may be dealing really with a number of different disorders, which may explain why patients react in different ways to the condition. If, indeed, a common denominator does exist between migraine and hypertension, the solution to this intriguing problem must, at least for the time being, remain unanswered. Though both migraine and hypertension are common conditions and must therefore frequently meet, the impression was gained that the association between the two conditions was more than one of chance.

Summary and Conclusions

The medical records of 5,785 patients in one general practice have been examined for a history of migraine. The incidence has been estimated as 4.85%. Of these patients, 54.8% gave a family history of migraine.

Patients with migraine were found to have a higher blood-pressure than the average for the population.

In patients over the age of 50 there was a clear and possibly direct correlation between migraine and essential hypertension. The incidence of migraine rose as the level of blood-pressure increased.

I am indebted to my former principal, Dr. C. G. Maxwell, for permission to conduct the investigation and to Dr. I. M. Richardson, department of public health and social medicine, Aberdeen University, for his interest in the work and for his advice and encouragement.

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"The Council wish that more [old people's] homes could be encouraged to allow residents to furnish their own room, or to bring articles of furniture where they must still share a bedroom. Living conditions must be improved. Administrative expediency seems to transcend the happiness of each resident when this subject is raised. Many committees and officials insist that residents prefer modern matching furniture to their own belongings. This may be the reaction if emphasis is put on how much nicer the new home and furniture looks, and many residents would be diffident, in such an atmosphere, of disagreeing and asking for their own possibly well-worn belongings. Only recently the secretary of Methodist Homes for the Aged was quoted as saying: 'We like our residents to have their own private room and they are allowed to bring in their own furniture.' The Methodists have 14 homes with 400 residents, and their experience covers a number of years. Their attitude of mind could be copied with advantage by many other homes." (*Annual Report for the year ending March 31, 1959*, National Old People's Welfare Council.)

DIAGNOSIS AND PROGNOSIS OF CAUDA EQUINA SYNDROME PRODUCED BY PROTRUSION OF LUMBAR DISK

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This paper draws attention to the poor prognosis for complete recovery of function in some patients with cauda equina syndrome due to compression by prolapse or extrusion of lumbar disk. The study of a comprehensive group of these patients in a neurological centre brings out two important points (1) the relative ease of arriving at an early diagnosis; and (2) that early operation is an essential prerequisite for improvement in prognosis.

Clinical Case Material

During a six-year period, 139 of the patients with "lumbar disk syndromes" admitted to the Maida Vale Hospital, under the care of Mr. Valentine Logue, were submitted to laminectomy. Many of them were operated on by me; 13 were suffering from cauda equina compression. The present paper concerns this group of 13, as in these cases there is maximal disturbance of neurological function, and delay in diagnosis and operation results in incomplete recovery of this function.

TABLE I.—*Clinical Case Material*

Patients operated on for "lumbar disk syndrome" during 6-year period ending May 31, 1957	139
Laminectomies performed	142
Compressing disk lesions found and removed	138
Neurofibromatous thickening of nerve root	2
"Negative" exploration	2
Posterior rhizotomy	1
Radiculysis	1

TABLE II.—*Analysis of Positive Disk Lesions*

Patients with positive disk lesions	136
Laterally situated lesions	97
Centrally	41
Patients with multiple lesions	2
Total compressing disk lesions	138
Patients with cauda equina syndrome and having central disk prolapse or extrusion	13

Tables I and II show that whereas the cauda equina syndrome occurs in less than one-tenth of the patients in this series, it was present in nearly one-third of those whose disk was central in position.

Manner of Involvement of the Cauda Equina

The cauda equina consists of all the anterior and posterior roots which leave the lumbar theca below the lower end of the spinal cord (opposite L 1–2 disk), so it comprises all the lumbar roots with the exception of the first and all the sacral and coccygeal roots. A "total" involvement of the cauda is most unusual, and such is not implied by the term "cauda equina syndrome." The term is used here to mean compression of the lower part of the cauda equina—as all except two of the compressions were at the L 4–5 level or lower. The two exceptions were at L 3–4 level.

In all cases involvement of the cauda equina at and below the level of the disk compression was incomplete. In some cases there was asymmetry of impairment of function as between the two sides, and in all there were differing degrees of disturbance of "motor, sensory, and sphincter" function.

As used in this paper the terms "motor" and "sensory" refer to limb supply only and "sphincter" refers to both motor and sensory supply to the bowel and bladder and not only to their sphincters. It is used as a convenient clinical term only, and is appropriately qualified in the text where necessary.

Motor Manifestations.—These included symptoms and signs of limb weakness or of weakness of some movement, evidence of hypotonia in the limb or some muscle groups, and diminished or absent reflexes.

Sensory Manifestations.—These comprised symptoms of numbness or various paraesthesiae and objective signs of sensory loss in a dermatomal and myotomal distribution.

Sphincter Involvement.—In respect of bladder function this took the form of difficult micturition or retention of urine; failure of appreciation of the filling of the viscus or loss of urethral sensation; and, in some cases, stress incontinence. The main bowel disturbance was constipation, and, in most cases, lack of appreciation of rectal distension and loss of anal sensation. Loss of sexual power occurred in some patients.

Classification of Patients: Features in Diagnosis

The 13 patients fall into two groups; group 1 comprising two cases (Nos. 1 and 2) and group 2 11 cases (Nos. 3 to 13).

Group 1.—In these two patients the syndrome developed slowly—over a period of six years in Case 1 and of one year in Case 2, remaining incomplete in both. There was no history of preceding injury or lifting strain; at operation only a diffuse backward bulge of the disk was found; and the prognosis was better than in the other cases.

Group 2.—These cases were characterized by the rapid development of some or all of the features of the cauda equina syndrome. In all cases this syndrome followed an episode of severe pain, and in all save one there was a history of injury, lifting, or twisting strain of the back. At operation the findings were characteristic, and the prognosis was not so good as in Cases 1 and 2. Improvement in results may be expected if the diagnosis is made and definitive surgical treatment carried out earlier. Therefore these cases are discussed in further detail.

Role of Injury or Back Strain.—Injury or back strain was present in all cases in group 2 except Case 3, and in most there were at least two distinct incidents—one before the onset of any back or limb symptoms and again before the onset of the cauda equina syndrome. The injury or strain prior to development of the syndrome was severe in seven patients and mild in two. It is not intended to suggest that such cauda equina syndromes are "traumatic" in origin but that in most cases of this type some lifting or twisting strain of the spine is associated with prolapse or extrusion of part of a disk already degenerated. Such history of injury is mainly of interest in differentiating between disk and tumour as the cause of cauda equina compression. (Jennett (1956) attaches less importance to the role of injury immediately preceding the onset of the cauda equina syndrome. However, such a history was obtained from 10 of the 11 patients.

Total Duration of All Symptoms.—This varied from 3 months to 15 years, with a mean of 5 years and 11 months. The symptoms consisted solely of back pain

in the lumbar region in six patients, back pain with radiating symptoms in five, and radiating symptoms only in two. In group 1 patients the cauda equina syndrome developed slowly during the whole period of the history (six years and one year respectively). In group 2, only one patient (Case 6) had a sudden onset of the syndrome without premonitory back or lower-limb symptoms. In the other 10 cases back or radiating symptoms preceded the onset of the syndrome by months or years, ranging from 2 months in Case 3 to 15 years in Case 4, giving a mean period for the preceding symptoms of six years and eight months.

Duration of the Syndrome.—The mean duration of symptoms of cauda equina compression in group 2 was 17 weeks. If the two neglected cases (Nos. 6 and 12) are excluded the mean duration was four weeks and two days—varying between five days in Cases 5 and 10, and seven weeks in Case 8. These periods differ markedly from group 1 cases, where the mean duration was 3½ years.

Rate of Development of the Syndrome.—This also showed a marked difference between the two groups. In group 1 the syndrome developed in a gradual manner, and in group 2 it came on relatively very quickly. The following criteria have been used to determine the presence of the syndrome: time of onset of urinary retention, numbness in the lower limbs, or (in those cases without sphincter or sensory symptoms) definite weakness of the legs. With these criteria it has proved possible to make an estimation, accurate within a few hours, of the time during which the cauda equina syndrome became established. Table III brings out the shortness of this period relative to the duration of the syndrome. It was 12 hours or less in five cases, 7 days or less in five, and in only one (Case 6) was the duration more than a week.

Time of Onset of Radiating Symptoms.—This was easier to establish with certainty and was taken to include radiating lower-limb pain, numbness, or tingling paraesthesiae. Table III shows that such symptoms occurred within a few minutes in 6 cases, within a few hours in two, and in less than a week in three.

TABLE III.—*Time Relations and Role of Injury in the Syndrome (Group 2)*

Case No.	Total Duration of Symptoms	Injury or Strain		Time Interval Between Pain or Strain and Onset of Radiating Symptoms	Period During which Syndrome Developed	Duration of Syndrome Before Operation
		Preceding Past History	Preceding Cauda Equina Syndrome			
3	3 months	Nil	Nil	12 hours	Within 12 hours	1 month
4	15 years	Yes	Yes	Few minutes	Within 1 week	6 weeks
5	11 months	,,	,,	,, ,,	Within 12 hours	5 days
6	2 years	,,	,,	,, days	Within 4 weeks	2 years
7	13 ,,	,,	,,	,, minutes	3 days	1 month
8	12 ,,	,,	,,	,, ,,	Within 12 hours	7 weeks
9	2 ,,	Nil	,,	2 days	4 days	10 days
10	4 ,,	,,	,,	Few minutes	Within 24 hours	5 ,,
11	13 ,,	,,	,,	,, hours	Within 12 hours	2 months
12	5 ,,	Yes	,,	,, minutes	,, ,,	10 ,,
13	3 ,,	,,	,,	6 days	6 days	6 weeks

TABLE IV.—*Summary of Clinical Features*

Case No.	Sex and Age	Occupation	Main Symptoms and Signs	Period of Sphincter Involvement	Returned to Work	Length of Follow-up
1	M 51	Labourer	M+S+Sph	2 years	3 mths. (L.W.)	6½ yrs.
2	M 48	Chemist	S+Sph	4 weeks	2 ,, (O.O.)	6 ,,
3	F 38	Housewife	M+S	—	4 ,, (L.W.)	3½ ,,
					8 ,, (O.O.)	
4	M 52	Shipping manager	M+S+Sph	5 weeks	4 ,, (O.O.)	3 ,,
5	M 33	Cinema projectionist	M+S+Sph	5 days	4 ,, (O.O.)	3½ ,,
6	M 53	Stock jobber ..	M+S+Sph	2 years	6 ,, (O.O.)	4 ,,
7	M 39	Tulip exporter ..	M	—	3 ,, (O.O.)	2½ ,,
8	M 42	Tool-setter	M+Sph	4 weeks	5 ,, (O.O.)	2 yrs. 2 mths.
9	F 36	Rubber packer ..	M+S+Sph	6 days	22 mths ; not returned	1 yr. 10 mths.
10	M 40	Baker	M+S+Sph	5 ,,	3 mths. (L.W.)	1 ,, 9 ,,
11	F 40	Housewife	S+Sph	2 months	6 ,, (L.W.)	1 ,, 7 ,,
12	M 50	Labourer (Cypriot)	M+S+Sph	10 ,,	Not known	—
13	M 41	Lathe turner ..	M	—	5 mths. (L.W.)	1 yr.

M=motor; S=sensory; Sph=sphincter; O.O.=original occupation; L.W.=lighter work.

Clinical Features

Most of these are brought out in Table IV. Only the more important features are discussed here.

Group 1.—The main impact of the compression in both patients was on the sensory roots and on the fibres to the bladder. There was no involvement of motor function in Case 2 and it was very slight in Case 1. Sphincter involvement was slight in both cases.

Group 2.—These cases fall naturally into two subgroups—with and without sphincter involvement. *Patients with sphincter involvement:*—In respect of the bladder this took the form of difficult micturition or retention in eight patients (Cases 4, 5, 6, 8, 9, 10, 11, and 12); six of these had altered bowel function and five had loss of urethral and anal sensation. Six of the patients with sphincter involvement also had motor and sensory symptoms and signs (Cases 4, 5, 6, 9, 10, and 12); one had sensory manifestations (Case 11), and one motor manifestations (Case 8). *Patients without sphincter involvement:*—There were three patients in this subgroup (Case 3 with sensory and motor features, and Cases 7 and 13 with motor manifestations only). The details of motor and sensory involvement are not shown in Table IV and are not given for the group as a whole; they are, however, described in the case reports.

Factors in Prognosis

Pain

Pain in the lumbar region of the spine and radiating in the distribution of sciatic or femoral nerves is present in most cases with this syndrome, and, while of value in making the diagnosis, requires consideration in prognosis. Pain may be absent from the outset (rare) or may disappear during the course of the illness (sometimes suddenly). This may be due to involvement of motor roots only—or to cessation of conduction in pain fibres. The latter is the more usual cause and is associated with objective sensory changes. Such cessation of conduction may be temporary if the roots are not destroyed, or permanent if there is such destruction. But in a particular patient there is no way of being sure which of these two possibilities exists—other than by the passage of time. Accordingly early operation should be the rule.

A good prognosis should not necessarily be given because of the absence or cessation of pain, as clearly in

some cases there is, in these circumstances, *progression* of the syndrome and therefore a worse prognosis. For example, in Case 6 there was complete disappearance of the pain (some weeks) after the onset of the syndrome. Had there been persistence of pain after the first operation failed to disclose the disk prolapse, presumably the patient would have demanded earlier reassessment of his problem (there was a two-year interval between the two operations). In Case 13 such improvement of pain did in fact cause delay in referring the patient for operation. In all patients with pain, rapid relief of this pain was obtained by operation.

Sphincters Involved

In *all* such patients there was incomplete return of normal micturition. In Cases 6 and 12 (syndrome present for two years and for 10 months respectively) automatic bladder function became established. Of all symptoms those of sphincter disturbance are the most important for assessing prognosis.

Sensory Disturbances

In all patients with sensory involvement there was little return of innervation—for example, Cases 1 and 5, in which examinations were made 6½ and 3¼ years after the operations. O'Connell (1950) gave an explanation for this persistence of sensory deficit—that is, the compression of the sensory-nerve root occurs central to the ganglion cells, so that regeneration of destroyed fibres cannot take place. The sensory deficit in disturbance of the sphincters is likewise more persistent than motor loss. So that, in the absence of awareness of bladder-filling, emptying of the viscus is possible owing to recovery of power in the bladder detrusor, assisted in the initial stages by manual compression (see report of Case 5).

Motor Involvement Only

There were two patients in this series (Cases 7 and 13) solely with motor involvement. In both a fair return of power took place before leaving hospital, but return to work was delayed for three and five months respectively. In these cases the syndrome was present four and six weeks before operation. Recovery was finally complete in Case 7; in Case 13 there was slight weakness of dorsiflexion of the left great toe one year after the operation.

Duration of Syndrome

If Cases 6 and 12 are excluded, the duration of the syndrome (within the time range of the remaining patients), if considered alone, is less important in prognosis than the presence of sphincter or sensory involvement. However, the duration of the syndrome need not be considered in isolation and should be assessed only in association with the other factors discussed above. In the slowly developing incomplete compression (Cases 1 and 2) the duration was not significant in the prognosis, being 6 years and 1 year and recovery occurring rapidly in both. In the neglected patients (Cases 6 and 12) the long duration of the syndrome with complete loss of voluntary bladder control will result in recurring inflammatory episodes (already present in Case 6) and shortening of life from eventual ascending urinary infection.

In the remaining nine patients the picture is not so clear. In Cases 5 and 10 the syndrome was present for five days before operation, and sphincter and sensory recovery have remained incomplete, whereas in Case 7 early return of function occurred though the syndrome had been present for one month. However, in this patient only motor roots were being compressed.

There can be no certainty on a clinical basis alone what proportion of nerve fibres (sensory, motor, or to sphincters) are destroyed at the initial prolapse or extrusion and in what proportion there is (potentially) only a temporary loss of function from compression or interference with blood supply. Therefore it is important to make the diagnosis and carry out the operation as early as possible.

If, in this series, at the time of operation, there had been some patients with syndromes present for 24 hours or less (and in six the syndrome developed within 24 hours) a more truly significant relation might have been drawn between duration and prognosis.

Incomplete Compression From a Slowly Developing Lesion

Patients with such lesions (Cases 1 and 2) have a relatively favourable prognosis. However, as can be seen from the report of Case 1, recovery is earlier and more complete in respect of motor power and longer delayed, and remains incomplete for sensory and sphincter function.

Case 1

This patient, a man of 51, had been a miner for 15 years and then a heavy labourer for 20 years. He had had lumbago for six years prior to admission, and during this period he noticed progressive weakness of his legs. In addition, he had attacks of increasing pain and numbness which came on while working—starting in his feet, radiating up the legs, and becoming so severe that he had to sit down for relief. The symptoms would then subside and he could resume working. Weakness was associated with these attacks, and in succeeding years the bouts of weakness, numbness, and pain on walking progressed in severity and came on after shorter distances, so that just before admission merely movement about his house brought on the attacks. He had difficulty in micturition and absence of anal sensation for two years.

Examination showed marked bilateral wasting of glutei, hamstrings, and calf and small foot muscles. with hypotonicity, weakness, and absent ankle-jerks; cutaneous sensibility was impaired in all sacral dermatomes. There was no evidence of vascular insufficiency in the lower limbs.

Myelography revealed a partial block at L 4–5, and at laminectomy Mr. Logue found a large central disk protrusion. This took the form of a diffuse backward bulge of the whole disk and there was no real extrusion of cartilage. The radiating symptoms quickly improved and were no longer present three months after operation. The power also quickly returned to normal in three months. Further recovery was only slight, but when last seen 6½ years after operation he could walk for long distances (for 4 to 6 miles; 6.5 to 10 km.) compared with 20 yards (18 metres) before the operation. He was still having a little difficulty with micturition. On examination at this time there was slight weakness of eversion of both feet. Sensation was more affected, there being marked hypalgesia in S 2 and 3 dermatomes and slight loss of pain in the fifth sacral dermatomes.

Comment.—This case illustrates the features of group 1 patients: absence of history of injury or spinal strain, slowly progressive development of the cauda equina syndrome, and good initial recovery.

Case 5

A cinema projectionist aged 33 first noted back pain 11 months before admission after lifting a heavy film projector. A prolapsed intervertebral disk was diagnosed at this time and treated with a surgical belt for three months with relief. Two further episodes of back pain occurred three months and two weeks prior to admission.

Five days before admission and following a jolt on his motor-cycle he noticed a similar pain in his back. On this occasion it persisted and was associated with bilateral sciatica and radiation into the buttocks. During the next 12 hours the pain became very severe indeed, with more widespread radiation into the legs and ankles. Morphine injections were given to relieve it and he was seen in a surgical out-patient department next day, when retention of urine had developed. He was referred back to his own doctor, who relieved the urinary retention by catheter. Constipation developed with the urinary retention and complete numbness in the saddle area. There was very little weakness of the legs.

Examination revealed obliteration of the lumbar lordosis, spasm in the erector spinae muscles, poor and painful spinal movement, and reduction of straight-leg raising to 45 degrees right and left. He had a symmetrical cauda equina syndrome involving all sacral segments on both sides, with hypalgesia in the first and second sacral dermatomes and analgesia in the third, fourth, and fifth dermatomes, including loss of urethral and anal sensation. Wasting, hypotonicity, and slight weakness of gluteal and hamstring muscles were apparent but no weakness of foot movements. Both ankle-jerks were absent. The myelogram showed complete block at the lower border of L 4 vertebral body (Fig. 1), and at operation I removed a disk extrusion measuring 2 by 1 by 1 cm. After operation the return of bladder function was slow, and on discharge from hospital six weeks later manual compression was still needed. After six months the sensation of bladder-filling had not yet returned, manual assistance was still required occasionally, and the saddle anaesthesia showed no obvious change. After one year there was still straining on micturition, troublesome constipation, and little change in sensation. This patient was seen twice more, 1½ and 3¼ years after operation. There had been no further significant change in symptoms, and examination showed the sensory change in the sacral dermatomes as before—that is, analgesia in S 3 to 5, hypalgesia in S 1 and 2. He had been rendered impotent by the disk extrusion and remained so. He was free from pain.

Comment.—This case illustrates a history of previous back pain, the role of back strain preceding the onset of symptoms of cauda equina compression, and the short time required for full development of the syndrome. Of interest also is the relative sparing of motor function with marked involvement of sensory, sphincter, and sexual function. In regard to prognosis it should be stressed that, though operation was done within five days, return of bladder function was still incomplete a year later, and sensory impairment was virtually unchanged over three years after the operation. The importance of testing sensation within the sacral dermatomes is well exemplified by this case (this can only be done adequately if the patient is in the prone position).

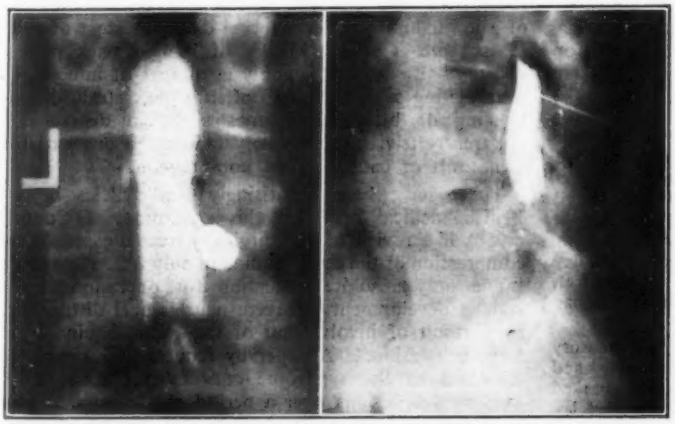

FIG. 1.—Myelogram showing complete block to downward flow of ethyl iodophenyl-undecylate opposite L 4–5 disk.

Case 8

A tool-setter aged 42 was admitted to hospital in November, 1955. He had had recurring attacks of low back pain for 12 years—four or five such attacks yearly, each lasting for some two to three weeks. He had sustained an initial severe jolt to the spine during the battle of Alamein, when he was thrown out of a dugout after a direct hit by a shell. Some of the subsequent episodes of pain he associated with small strains, such as coughing, sitting up, stepping off a kerb, etc.

The attack which culminated in his cauda equina syndrome began seven weeks before admission. On getting out of bed one morning and on attempting to gain the erect position he had a sudden pain in his back, with immediate radiation down both legs to the feet accompanied by a numb sensation. Acute retention of urine developed later, and he was admitted to another hospital and treated for acute prolapsed intervertebral disk. Urinary retention proved to be of short duration. He was treated by catheter and was later referred to another hospital under the care of a neurologist. Examination there showed wasting of calf and anterior tibial muscles of both legs, with hypotonicity and marked weakness resulting in bilateral foot-drop and loss of ankle-jerks. Disturbance of cutaneous sensibility was minimal—hyperpathia to pin-prick in all the sacral segments but no actual loss of sensation.

Myelography revealed a large anteriorly situated lesion opposite the L 4–5 disk space. Mr. Logue felt there had been a massive extrusion of the L 4–5 disk, and on December 3 carried out laminectomy. An extensive prolapse of this disk was found, with several large necrotic fragments of cartilage within it. The disk protrusion was estimated to be the size of a marble and had produced a tight compression of the lower part of the lumbar theca and cauda equina.

The post-operative and subsequent course was favourable. The position became static about five months after operation. Since that time he has had minor complaints only—very slight pain in the back and radiating tingling sensation from feet to knees. He was last seen 2 years and 2 months after operation, when there was almost complete return of power—there still being slight weakness of extension of the left ankle and hallux. The ankle-jerks were still absent and there was hypaesthesia in L 5–S 1 dermatomes bilaterally.

Comment.—This case illustrates the role of injury, the long preceding history, and the suddenness of onset of the cauda equina compression. The severity of involvement of the motor fibres, with almost complete escape of sensory roots and of bladder function, is of interest, especially in view of the tight compression found at operation. The relatively good prognosis with almost full recovery in five months is worthy

of comment, even though the lesion had been present for seven weeks before operation.

Case 13

This patient, a metal lathe turner aged 41, doing heavy work, had had occasional episodes of lumbago for years.

One morning, doing a twisting movement, he felt "something pop in my back." There was a little mild pain, which built up during the course of the morning and became so severe that at lunch-time he returned home and went to bed. The pain continued for six days, when for the first time he noticed weakness of his legs. This weakness progressed rapidly and was accompanied by cramps in his calves. Later the pain became intense, radiating down the whole of the right leg and to a less degree down the left leg. His legs were so weak that he had to be helped to bed. His doctor visited him the next day and diagnosed a prolapsed disk. There followed a fortnight of delay before admission to hospital. The pain was severe during this period and was aggravated by coughing or sneezing.

In hospital he was put on fracture boards for two weeks and then encouraged to get up for a further week. His pain improved greatly but the legs remained weak. Other sensory symptoms or signs did not appear and the sphincters were not involved. After about a month he was seen by a neurologist, who arranged for immediate transfer to the Maida Vale Hospital in February, 1957.

Examination revealed a flaccid paraparesis involving gluteal, hamstring, and especially flexor and extensor groups of both legs. There was slight weakness of the quadriceps on both sides, but the knee-jerks were present. The ankle-jerks were absent. There were no sensory signs.

A myelogram revealed an almost complete block at the lower border of L 3, and at laminectomy an extruded portion of disk (5 by 0.5 cm.) was removed. This was curled up and pressing back into the theca and had gone from the L 3–4 disk through a small hole in the thinned annulus and posterior common ligament. There was no disturbance of bladder or sensory function post-operatively. Recovery of motor-power was relatively rapid and on discharge from hospital five weeks after the operation he was able to walk, though with a waddling, shuffling gait. However, he did not return to work for five months and did not regain full use of the legs until nine months after operation. When last seen, one year post-operatively, there was very slight weakness of dorsiflexion of the left great toe as a remnant of his neurological disability.

Comment.—This case illustrates the selective involvement of the cauda equina and the more favourable prognosis when the nerve supply to the sphincters and the sensory roots are not involved clinically. The relative freedom from pain and lack of bladder and sensory disturbance may have had a bearing on the lamentable delay in arranging transfer for operation.

Case 9

This patient aged 36, was a housewife and part-time worker in a rubber factory. Two years previously she had a single attack of right sciatica. Ten days before admission to hospital she suffered sudden low backache. This cleared for a day, then returned and persisted. After four days it was associated with radiating pain in the right lower limb. On the same day retention of urine was noted. Next day tingling paraesthesiae and weakness appeared in both feet. For two weeks immediately preceding this episode she had been nursing her bedridden mother.

Examination revealed symmetrical motor and sensory involvement of the cauda equina with flaccidity and weakness of all muscles below the knees, less marked wasting, and weakness of gluteal and hamstring muscles. Marked diminution of all forms of sensation was found in all the sacral dermatomes. Urinary retention and constipation were evident. A myelogram revealed a complete block opposite the body of L 4.

At operation I removed two large necrotic fragments of disk, lying free in the spinal canal. These had extruded from the L 4–5 disk and had extended up the canal to lie above the disk level.

About a month after operation micturition had become relatively normal. Power returned to the limbs much more slowly and there was virtually no change in sensation. When seen 1 year and 10 months after operation she had not returned to her employment in the rubber factory and required the assistance of a stick and leg-iron for walking. On examination the proximal muscle groups (gluteal and hamstrings) had regained their bulk and power. The distal muscles were very weak. Sensation was virtually unchanged from the pre-operative state.

Comment.—This case illustrates the poor prognosis in some cases. It is especially so when the sphincters and sensation are involved in addition to motor loss.

Discussion

Diagnosis of the cauda equina syndrome can be made by evaluation of the history and by clinical examination. When such a lesion is suspected judicious inquiry should be made for symptoms indicating compression of lumbar or sacral nerve roots. The most important of these are: weakness of muscles below the knees, impairment of skin sensation in the saddle area, difficult micturition, and radiating symptoms. Radiating symptoms consist of pain, tingling, and other paraesthesiae or numbness. Constipation may go unnoticed if it represents little change in the patient's usual bowel habit.

Examination will be directed especially towards the spine, lumbar and sacral skin and muscle segments, and the bladder. The only way of examining the sacral segments adequately is with the patient prone. Even small degrees of wasting of the buttocks will be apparent; loss of tone, weakness of the gluteal muscles, and sensory loss in the sacral dermatomes can be readily demonstrated. One or both ankle-jerks are absent in most of these cases. A distended bladder not uncommonly escapes casual observation.

The cauda equina syndrome is only very rarely complete—in disk cases, only the lower lumbar, sacral, and coccygeal roots being involved—and is often asymmetrical in regard both to right and left sides and to manner of involvement of "motor," "sensory," and "sphincter" supply. The most common, and remediable, cause of the syndrome is central prolapse of a lower lumbar intervertebral disk. In most of such cases there is a long history of lumbar back pain—constantly or more commonly as attacks of lumbago—or radiating symptoms, and often a back strain due to twisting or lifting, sometimes slight in degree and apparently trivial, immediately before the onset of the symptoms of cauda equina compression.

There have been surprisingly few articles in the British medical press on this syndrome. O'Connell (1950), in a review of 500 surgically treated cases, found compression of the cauda equina in only 2%. He wrote: "The only absolute indication for operation is the sudden development of severe neurological disturbance as a result of involvement of the cauda equina by a large protrusion." A paper by Jennett (1956) reported 25 cases of the syndrome culled from about 1,000 verified disk lesions over a period of 18 years. These two papers contain reviews of the more important publications on the subject up to 1956.

The number of patients in the present series represents a high incidence relative to the total number of patients suffering from lumbar disk disease. The incidence is also high compared with other series. This may be due to the method of reference of patients with disk disease to the neurosurgical unit of the Maida Vale Hospital. All in this series had been examined by one or more consultants before transfer.

However, the cauda equina syndrome as produced by lumbar disk prolapse or extrusion is not so rare as is generally supposed. In the first nine months' tenure of my present appointment I have had three patients suffering from this syndrome referred to my care. Fig. 2 is a photograph of a "disk sequestrum" removed at operation from the last of these patients.

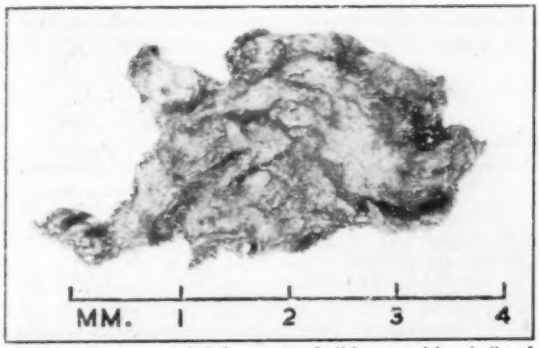

FIG. 2.—Single extruded fragment of disk comprising bulk of nucleus pulposus.

Mention is required of the association of manipulation and the cauda equina syndrome. Such a manœuvre precipitated the onset of the syndrome in one patient in this series. If there is any evidence to suggest a central disk prolapse not yet producing a cauda equina syndrome, manipulation should be avoided. The finding at operation in a number of these patients of a thinned annulus and posterior common ligament, and the fact that so many of the frank cases of the syndrome follow relatively trivial traumata—acting on an already diseased disk—indicate the danger of manipulation.

The profound disturbance of function which follows acute central prolapse or extrusion of a lumbar disk is clear from a study of the patients forming the basis of this paper. The slow return of this function, with delay in diagnosis and operation, is also apparent. These lesions do not of themselves endanger life. However, when no relief is afforded, the paralysis of bladder and sensory function leads to ascending urinary infection and decubitus ulcer formation, and so result in a shortening of the life-span. Uraemia or septic absorption from bed-sores brings to an early end a miserable and limited existence.

Summary

In order to improve the prognosis attention is drawn to the need for early diagnosis and operative treatment of patients with the cauda equina syndrome due to lumbar central disk prolapse or extrusion.

Thirteen patients have been chosen for study, being nearly one-third of those having central lumbar disk lesions and one-tenth of those with compressing disk lesions verified at operation and seen over a six-year period.

The 13 patients are classified into two groups. The main diagnostic features are described, the role of injury and the rapid development of the syndrome in most cases being specially stressed.

The manner in which the cauda equina may be involved is described.

Factors in prognosis are mentioned: pain; sphincter, sensory, and motor involvement; and duration of the syndrome. Their relative importance is discussed.

Five illustrative case-histories are given, and the main clinical features of the whole series are tabulated.

The discussion includes remarks concerning the diagnosis and frequency of the syndrome. The possible danger of manipulation is mentioned and allusion made to the plight of the unrelieved sufferer from this condition.

I thank Mr. Valentine Logue for granting me access to his personal notes of these patients and for allowing me to perform many of the operations. I am indebted to Dr. D. Sutton for permitting me to include Fig. 1. My thanks are due to the medical committee of the Maida Vale Hospital for allowing me to publish. I am grateful to Mrs. Davis for secretarial assistance.

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PULSELESS DISEASE, OR TAKAYASHU'S DISEASE

CASE REPORT

BY

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Cases of unilateral absence of pulse due to aortic aneurysm have been known since 1757, when William Hunter described the condition, but bilateral absence of the arterial pulses is exceedingly rare. In 1908 Takayashu reported a peculiar case with cataracta complicata and unusual ocular findings. At the meeting at which the case was described Onishi and Kagoshima reported two similar cases, with the addition that radial pulsation was absent in one of the patients. It was not, however, until the review by Shimizu and Sano (1953) that this pulseless-disease–aortic-arch syndrome, or reversed coarctation, became recognized by Japanese ophthalmologists as a rare but definite entity. Since that time 69 cases have been reported from Japan, and 34 from Europe and America, including several in recent years. The present paper records a further case, the first one from India.

Clinical Signs and Symptoms

Clinically, pulseless disease is characterized by three cardinal signs; the most common is absence of palpable

arterial pulsation in the upper extremities, in the carotid, and in the superficial temporal arteries. The other two signs are peripapillary arteriovenous anastomoses and microaneurysms, and a hypersensitive carotid sinus which frequently cause attacks of syncope and vertigo. Two additional signs often considered classical are the development of cataract and the absence of blood-pressure in the upper limbs. Syncopal attacks are frequently associated with convulsion, and sometimes are followed by transient hemiparesis.

Other reported ocular findings are obliteration or irregularity of arteries in the periphery of the retina, with clumping of blood and pallor of the fundus, mydriasis, iris atrophy, dilatation of conjunctival and episcleral vessels, pigmented deposits on the back of the cornea, retinal and vitreous haemorrhages, retinitis proliferans, and very low central artery blood-pressure. Dodo (1950) therefore applied the term "ophthalmo-angiopathica-hypotonica" to these ocular manifestations.

In addition to these ocular findings, the following have been noted: delicate skin; fine poorly pigmented hair; attacks of syncope; intermittent claudication in the upper limbs, but rarely gangrene; speech disturbance; pulsation of subcutaneous arteries over the back, chest, and upper abdomen; attacks of pain in the orbit, eyeball, and chest; hemiplegia; hypomenorrhoea and amenorrhoea. The most common early symptom is recurrent transient blurring of vision, especially when turning the face upwards or quickly assuming an upright position. These patients often hold their head, with the face directed downwards, as they find that vision is thereby often improved because of the increased blood supply to this area. A high blood-pressure in the legs has been reported in about half the cases. Ross and McKusick (1953) quote convincing experimental evidence and suggest that hypertension arises from progressive cerebral ischaemia. The disease slowly worsens, and after a period of blindness death usually ensues from cerebral infarction.

Aetiology

Pulseless disease has a predilection for young females, who outnumber males by 10 to 1. It is seen during or after puberty. An acute infection, such as scarlet fever or tonsillitis, may precede the onset of the disease.

There appear to be two definite forms of pulseless disease. One is associated with pathological findings compatible with syphilitic aortitis at post-mortem examination. The other is more common in females, and fits more closely Takayashu's description of the disease. In these cases the serological test is negative. Post-mortem examination has been reported in only six of the non-syphilitic cases. The pathological process was restricted to large arteries close to their origin, and consisted of thickening and hardening of the adventitia, disruption of elastic lamellae of media by collagenous connective tissue, and infiltration by round cells and plasma cells; intima was thickened by atheromatous plaques, and the lumen occluded by organized thrombus. Biopsy of peripheral vessels revealed simple narrowing due to diminished blood flow, but there was no sign of arteritis. As an aid to diagnosis, the site of obstruction of the brachiocephalic trunks at their origin can be confirmed by aortography.

The cause of the condition is obscure. The sedimentation rate is high, and the presence of lupus erythematosus (L.E.) cells has not been reported. Probably the disorder is caused by non-specific arteritis at an unusual site. Shimizu and Sano (1953) felt that histologically the picture was suggestive of a tuberculous lesion, and the presence of Langhans giant cells was noted; however, no organisms were found by smear, by guinea-pig inoculation, or by culture.

Other theories advanced as the cause of the second group of cases include Buerger's disease, allergy, panarteritis of unknown aetiology, and collagen disease.

Pathological Physiology

The fundamental lesion is an occlusion of the great vessels, usually the brachio-cephalic trunks or subclavian and carotid arteries close to their origin from the aorta, with consequent ischaemia of the brain, eyes, and upper limbs (Fig. 1). To compensate for the diminished blood supply there is a development in the collateral system. The collateral blood supply to the face is often sufficient to provide the necessary nutritive material. This is done by way of the subclavian artery to the thyroid gland, on to the superior thyroid artery, then to the external carotid and the vessels of the face. The enlarged thyroid in pulseless disease may result from this process.

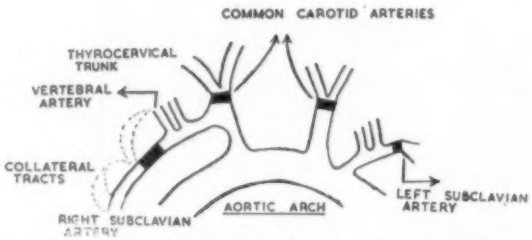

FIG. 1.—Diagram showing probable site of lesion in pulseless disease.

The collateral blood supply to the brain via the vertebral arteries of the circle of Willis, then to the middle cerebral and anterior cerebral arteries, is often insufficient and may result in hemiparesis and loss of memory. Because of this, nutrition to the eyes is also affected and may result in structural atrophy, especially of the retina.

The collateral blood supply to the upper limbs via the pectoral branch of the thyro-cervical trunk on to the thoraco-dorsal artery of the humerus and thence to the deep brachial artery is usually sufficient for nutrition of this area. A continuous murmur may be audible over large collateral vessels, and in the neck over main arteries, owing to post-stenotic dilatation.

Whenever there is a constant and greatly decreased arterial pressure, such as is found in the retinal arterioles, the finer capillary channels are short-circuited and arteriovenous anastomoses occur, thus explaining the early arteriovenous anastomosis in the periphery of the retina and the large arteriovenous anastomosis seen around the optic nerve head in the late stages of the disease. The clubbing of the fingers and the arteriovenous anastomosis in the tips of the fingers sometimes seen can be explained in a similar manner. Because of the decreased blood supply to the area, a lowered arterial pressure in the retinal arteries can be easily demonstrated by pressure on the globe.

and may be an early finding of pulseless disease. Cataract formation can also be explained because of decreased nutrition, which also leads to gradual atrophy of the peripheral retinal elements.

Attacks of dizziness, convulsions, or unconsciousness seem to be associated with a hypersensitive carotid sinus and are often produced merely by the patient stretching his neck, or by pressure on the carotid sinus. The hypersensitivity of the carotid sinus is explained on the basis of an insufficient blood supply to this area over a long period. Pinkham (1955) and De Bes *et al.* (1955) reported the following findings in the eye:

Lens: Coagulation necrosis. Ciliary body: Atrophy of muscle and ciliary processes. Retina: Clumping of rods and cones; decrease in number of ganglion cells; formation of new vessels in nerve fibre layers. Central retinal artery: Marked proliferation of the intima. Optic nerve: Demyelinization.

Differential Diagnosis: Prognosis

Temporal arteritis, Buerger's disease, and panarteritis nodosa may be considered in differential diagnosis, but these can be easily differentiated and ruled out.

The prognosis is poor, though some patients can carry on, with limited activity, if their collateral circulation to the brain is sufficient. As regards vision, prognosis is unfavourable. In a few cases cataract extraction has been done, only to reveal an atrophic retina with poor perception of light. The course of the disease ranges from 1½ to 14 years. Death may result from chronic debility due to cerebral ischaemia, though it may be the result of myocardial disease.

Treatment

No known treatment is effective. Caccamise *et al.* (1952, 1954) have suggested that cortisone and corticotrophin may be of value if treatment is initiated before irreversible changes have occurred; therefore cortisone and anticoagulant therapy is worth a trial in early phases of the disease. Lessof (1958) reports considerable physiological and symptomatc improvement in a patient on prednisolone treatment. A thrombectomy performed through the external carotid artery, coupled with denervation of the carotid sinus and removal of the carotid body, has been tried by Shimizu and Sano (1953) with some relief of symptoms. In another case they tried grafting of a piece of vein into the area where the thrombosis had been resected. This relieved the attacks of syncope, but there still appeared to be little flow of blood to the brain through this segment. Ross and McKusick (1953) described the successful relief of distressing syncope by resection of the carotid sinus. Sympathectomy of the cervical sympathetic ganglion has also been tried, but with poor results.

Case Report

A Hindu female, aged 27, was admitted to hospital on May 6, 1958, with a history of attacks of fainting fits for a year and diminution of vision for 20 days.

Nearly one and a half years previously she had intermittent headache on one side, and the eye on this side became red, but since the fainting attacks started the headache has subsided. The fainting is precipitated on getting up from a lying-down position, on looking up again, and on attempting to unlock or open the *Kundi* of the doors of the house. At first she used to fall many times and hurt herself during the attack of fainting, but she has now learnt to sit down or lie down at the onset of the attacks. If she puts her hand under her head or pillow while resting, the fingers become numb and flexed.

Past History.—She had typhoid fever in 1947. There was no history of rheumatic pain. Last year she was admitted to the general hospital, and the absence of a pulse was thought to be due to weakness and debility.

General Examination

The patient was a young, slightly built woman, who looked more than her age. Married 10 years ago. Two children, both healthy. The eyes appeared to some extent enophthalmic. Heart slightly enlarged, but sounds normal. Radial, brachial, and temporal arteries not palpable, and without pulsation. Blood pressure could not be recorded in the upper limb, but in the lower limb (popliteal artery) it was 230/90. Bruits audible on right side of chest in front, ½ in. (1.3 cm.) above and external to the mid-clavicular line and on either side of the back in the ninth intercostal space 4 in. (10 cm.) from the midline.

Eye Examination

She had perilimbal injection with some prominence of conjunctival and episcleral vessels. The cornea had pigmented deposits over its posterior surface, more on the right side. Both pupils were dilated, and sluggish to light and convergence. The iris was atrophic and showed many vessels, mostly in the ciliary part (different from rubeosis of diabetes, etc.). Tensions were: right side, 27 mm. Hg; left, 25 mm. (Schiøtz). Gonioscopic examination revealed vessels in the angle, which was very narrow and had some pigment deposits.

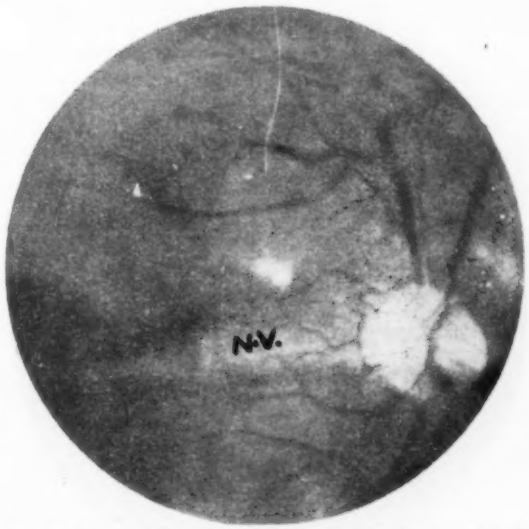

FIG 2.—Fundus photograph of right side showing new vessels (N.V.) near the disk, with somewhat dilated veins.

Fundus.—Right disk was covered with new blood vessels anastomosing between themselves (Fig. 2). A patch of proliferative retinopathy extended from the temporal side of the disk to the macula in the form of a broken girdle (Fig. 3). Veins were tortuous; arteries were contracted, with faint pulsation, and at places showed microaneurysms and arteriovenous anastomoses (Fig. 3). Vessels could not be traced up to the periphery, which was pale. The veins on the left side were tortuous and prominent. Many arteriovenous anastomoses were seen, with new vessels near the disk (Fig. 4). Some of the vessels on both sides showed

peri-sheathing and were obliterated. Pressure in the central arteries was observed by ophthalmodynamometer and found to be very low.

Laboratory Examination

Urine, total and differential W.B.C., and W.R. were normal; E.S.R. was 18 mm. in one hour; haemoglobin was 65%. *X*-ray films of the chest showed slight enlargement of the heart. Patient was given local cortisone drops, and prescribed "deltacortril" tablets with not much relief.

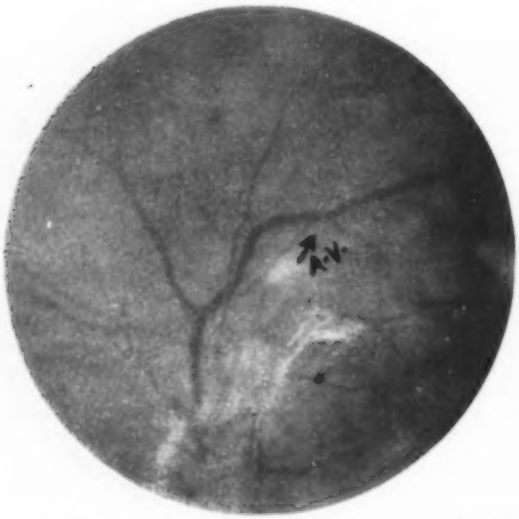

FIG. 3.—Fundus photograph of right side showing arteriovenous aneurysms and patch of proliferated retinopathy extending from temporal side of disk.

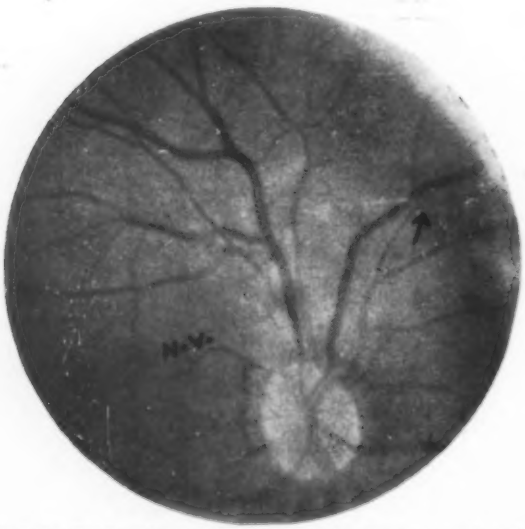

FIG. 4.—Fundus photograph of left side showing new vessels and arteriovenous aneurysms.

The patient came to this hospital again on July 20, 1958, with the history of attacks of headache on one or other side, lasting for a day or two. She also complained of total loss of vision in the right eye. On examination the right pupil was dilated and had mature cataract (duration 14 days). Vision in the left eye was 2/60, with early vacuolation in the lens cortex as seen by slit-lamp. The whole fundus, including the disk was pale. The vessels, particularly the arteries, were very attenuated; they became indiscernible as we traced them towards the periphery, and were completely invisible even before the equator. Loupes of new vessels were present near the disk. Perivascular sheathing, and even obliteration of the arteries, were now quite obvious.

The patient returned on November 26, 1958, with total loss of vision in both eyes, and cataract had developed in the second eye also. Pupils were dilated and fixed, with perception of light only. Cataract extraction (extracapsular, due to raised tension) was done, but under small peripheral iridectomy the iris bled because of the vascularization, and took a long time to absorb. The fundus was pale and there were many arteriovenous vessels near the disk. Cataract extraction did not improve her sight.

Summary

A typical case of pulseless disease in a young woman, the first from India, is described, with typical fundus changes, absent pulsation in the upper limbs, cataracts, attacks of syncope, and raised blood pressure in the lower limbs, with tendency to rise of ocular tension, probably due to new vessels and pigment deposits in the angle of the anterior chamber. The case passed on to complete blindness, though cataracts were removed successfully.

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"Most men of science would disclaim any great concern with philosophy and especially with metaphysics. But what is metaphysics? In the last resort it is the search for a statement subsuming the ultimate nature of all reality. Science has more modest hopes, and modern physics led the way to a considerable renunciation in this respect which has had a profound influence on philosophy itself. Yet in science the total neglect of philosophical aspects may be unfortunate. It can lead, on the one hand, to statements which are sensational but unsound, and, on the other, to an unhealthy indifference to the relationship of science to existence in general. And in any event, even though science may seem to decline metaphysical statements, it not only throws out challenges to philosophy but is frequently itself confronted with problems inescapably philosophical in nature." (Anniversary address by Sir Cyril Hinshelwood, P.R.S., November 30.)

BODY-BUILD OF MALE HOMOSEXUALS

BY

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Studies of the body-build of homosexual patients have produced conflicting reports. Weil (1924), in Germany, reported that homosexuals had a narrower biacromial diameter and a wider intertrochanteric diameter than a control group had. The latter unfortunately was obtained from a different part of the country and measured by a different observer. Wortis (1937) could find no abnormality in the body-build of homosexuals. Sheldon (1949) found there are no distinctive features of homosexual physique recognizable from a somatotyping photograph. He states, however, that the majority of homosexuals are recognizable by what he terms secondary gynandromorphy—that is, "the measures of the femininity of the face, hands, skin, and skin appendages; manner of movement and co-ordination; voice and facial behaviour; in short, the covert gynandromorphy that escapes the photograph." This is in agreement with the common clinical impression that the effeminate appearance that many male homosexuals show is the result of mannerisms of gait and dress affected consciously or unconsciously by the subject rather than due to any abnormality of body-build.

The present investigation was undertaken to determine whether homosexuals have an abnormal discriminant androgyny score—an index of body-build—which, as is shown below, is related to the sexual development of the individual. The discriminant androgyny score (Tanner, 1951, 1955) of a patient is obtained by measuring the biacromial and bi-iliac diameters and substituting in the following formula:

$$3 \times \text{biacromial} - 1 \times \text{bi-iliac diameters (in cm.)}$$

The term androgyny may be defined as the presence of android features in a woman and gynaecoid features in a man. Tanner obtained a score of 90.1 with a standard deviation of 4.75 for men; the comparable figures for women were 78.9 and 4.57. This sex difference in physique arises at puberty, and before this age the androgyny score fails to discriminate between the sexes.

There is evidence that the androgyny score, or its most important component the biacromial diameter, is correlated with sexual characteristics and abnormalities. Ferriman *et al.* (1957) found that women with hirsuties had an increased urinary 17-ketosteroids output, a tendency to oligomenorrhoea, and an increased biacromial diameter. Raboch (1957) found a decreased biacromial diameter in hypogonadal men and in men with female sex chromatin. Lindegård (1956) showed that size of penis was correlated with the androgyny score. Patients suffering from pre-eclamptic toxaemia and frigidity have been found to have abnormally masculine androgyny scores (Coppen, 1958). Thus there is evidence that subjects who suffer from certain abnormalities related to sexual function will show abnormalities in their androgyny score. The hypothesis tested in the present investigation is that homosexuals have abnormally feminine androgyny scores.

A second androgyny score was used in the present series. This was based on the relative thickness of subcutaneous fat and bone of the calf obtained from a soft-tissue *x*-ray film, and will be referred to as the fat–bone index of the calf (Reynolds, 1949; Tanner, 1955). This score is obtained by substituting in the following formula:

$$1 \times \text{bone diameter (mm.)} - 0.4 \times \text{fat diameter (mm.)}$$

The measurements are made at the maximum diameter of the calf. The index differentiates the sexes better than the discriminant androgyny score and misclassifies only 5% of a normal population of men and women (Tanner, 1955). This sex difference also arises at puberty.

The Investigation

Three groups of subjects were investigated: a group of homosexual patients, a control group, and a group of neurotic patients. The control group consisted of the members of a department of a large business organization who were attending for mass radiography. Over 90% of the department attended for the *x*-ray examination and all of these agreed to be examined for the purpose of the present investigation. The homosexual group consisted of 31 patients who had been either exclusively homosexual or predominantly homosexual, with only occasional heterosexual activity. The patients had attended the Maudsley Hospital primarily for homosexuality; the majority had been referred from the courts after they had been convicted of homosexual offences. Psychiatric symptoms—mainly depression or anxiety—were present to a varying extent in these patients but in none to a severe degree. However, in view of this another control group of 22 heterosexual neurotics was studied, as any differences found in the homosexuals may be related to the differences widely reported in psychiatric patients rather than to their specific sexual abnormalities.

All measurements were performed by myself, using a Martin anthropometer; the patients were measured standing, their shoulders relaxed. The *x*-ray films of the calf were taken as described by Tanner (1955).

The results are presented in Tables I–IV and the Chart.

TABLE I.—*Body Measurements in the Control, Homosexual, and Neurotic Groups; Comparison of Homosexual and Neurotic Groups With the Control Group*

Group	No.	Mean	S.D.	Compared with Control Group	
				t	P
Control	53				
Androgyny score		90·3	4·1		
Biacromial diameter (cm.)		39·8	1·7		
Bi-iliac diameter (cm.)		29·3	1·3		
Weight (kg.)		71·9	7·6		
Height (cm.)		172·6	6·1		
Age (years)		41·5	10·5		
Fat–bone index	10	35·2	4·4		
Homosexuals	31				
Androgyny score		88·5	5·6	1·68*	0·05
Biacromial diameter (cm.)		39·1	2·0	1·68*	0·05
Bi-iliac diameter (cm.)		28·8	2·2	0·71	Not significant
Weight (kg.)		73·0	10·8	0·54	" "
Height (cm.)		172·5	7·9	0·07	" "
Age (years)		40·0	9·7	0·65	" "
Fat–bone index		34·6	3·1	0·47	" "
Neurotic patients	22				
Androgyny score		88·4	4·8	1·74	Not significant
Biacromial diameter (cm.)		38·9	1·9	2·26	0·05
Bi-iliac diameter (cm.)		28·3	1·0	3·17	0·01
Weight (kg.)		66·7	9·8	2·50	0·02
Height (cm.)		173·6	6·7	0·70	Not significant
Age (years)		35·1	11·8	2·37	0·05

* One tailed test.

Correlation coefficient between androgyny score and fat–bone index 0·26—not significant.

TABLE II.—*Distribution of Subjects and Mean Androgyny Score According to Social Class*

Social Class	I	II	III	IV	V
Controls ..	(7) 92·6	(0)	(46) 90·1	(0)	(0)
Homosexuals ..	(0)	(8) 89·3	(15) 87·0	(7) 90·7	(1) 89·7

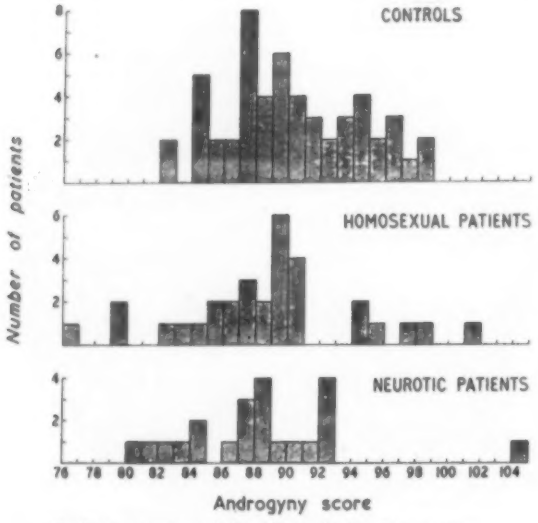
Number of patients in parentheses.

TABLE III.—*Results in Subjects Belonging to Social Class III*

	Mean	S.D.	Compared with Homosexuals	
			t	P
Controls (46):				
Androgyny score ..	90·1	3·2	2·78	0·01
Biacromial diameter (cm.)	39·7	1·8	2·17	0·05
Bi-iliac diameter (cm.)	29·5	1·6	1·71	Not significant
Age (years)	43·1	10·7	0·71	,, ,,
Height (cm.) ..	172·2	5·6	0·36	,, ,,
Weight (kg.)	71·5	8·6	0·26	,, ,,
Homosexuals (15):				
Androgyny score ..	87·0	3·1		
Biacromial diameter (cm.) ..	38·5	2·26		
Bi-iliac diameter (cm.)	28·6	2·15		
Age (years)	40·8	11·7		
Height cm.)	171·6	5·2		
Weight (kg.)	71·5	10·7		

TABLE IV.—*Homosexual Patients Divided Into Two Groups of Patients With and Without Other Psychiatric Symptoms*

	Without Other Psychiatric Symptoms (18)		With Other Psychiatric Symptoms (13)	
	Mean	S.D.	Mean	S.D.
Androgyny score ..	88·1	4·9	89·1	3·1
Biacromial diameter(cm.)	38·6	1·3	39·6	2·0
Bi-iliac diameter (cm.) ..	27·9	2·0	29·7	2·1
Age (years)	42·1	12·1	36·2	10·3
Height (m.)	170·1	5·5	174·8	9·8
Weight (kg.)	69·8	10·1	76·9	10·7


CONTROLS
HOMOSEXUAL PATIENTS
NEUROTIC PATIENTS
Number of patients
76 78 80 82 84 86 88 90 92 94 96 98 100 102 104
Androgyny score

Androgyny scores of the subjects in the three groups.

Discriminant Androgyny Score

Homosexuals differ from the controls in their biacromial diameter and androgyny score. There is no difference between the groups so far as the bi-iliac diameter, weight, height, and age are concerned. Because of the differences in body-build between subjects in different social classes that have been reported (Clements and Pickett, 1954; Board of Trade, 1957) both controls and homosexual patients were divided into five social classes according to the classification of the Registrar-General (General Register Office, 1956). Both the control and the homosexual group have the greatest number of patients in social class III. Table III shows that when patients of this social class are compared with controls of the same class the difference between the group is increased. Moreover, if there are differences due to social class factors between the controls and the homosexual group one would expect to see this reflected in differences in stature between the groups, whereas the mean height of the two groups is almost identical. Indeed, Clements and Pickett (1954) have shown that differences in chest girth between social classes disappeared when standardized for a constant stature.

The homosexual group was divided into two groups, one consisting of patients who complained of some other psychiatric symptoms, the other of patients who appeared free of other symptoms. Table IV shows there was little difference between these two groups; indeed, the patients with no other symptoms differed from the controls more than did the group with other psychiatric symptoms. This suggests that the difference in body-build found in the homosexual group is not related to the presence of these other symptoms.

The neurotic group has an androgyny score and a biacromial diameter very similar to the homosexual group, and in addition has a decreased bi-iliac diameter.

Fat-bone Index

The fat–bone index in the patients and that in the controls are shown in Table I. There is no difference between the homosexuals and the controls. There is no correlation between the fat–bone index and the androgyny score.

Discussion

The results show that homosexuals have a decreased androgyny score and biacromial diameter compared with the control group. This difference, however, is not specific for homosexuality, as the neurotic patients in this study also differ from the controls to approximately the same extent as regards both androgyny and biacromial width. The androgyny score does not discriminate between homosexuals and controls better than does the biacromial diameter, though, as the Chart shows, three homosexual patients have very low androgyny scores, outside the range of the other two groups. It appears, therefore, that homosexuals are similar to people with other psychiatric disorders in having decreased breadth measurements (Rees and Eysenck, 1945), but that their sexual abnormality is not specifically related to these. Rather it seems that the homosexual is influenced by the similar (unknown) factors that produce the abnormalities in body-build found in other psychiatric patients.

The androgyny score is unrelated to the fat–bone index. As both these sexual differences arise at puberty it might have been expected that both would be depedent on the same factors and hence related. However, the androgyny score is dependent on skeletal development alone, whereas the fat–bone index is dependent on soft-tissue development as well as bone.

Summary

The discriminant androgyny score, a measure of physique related to sexual development, was obtained on a group of 31 male homosexuals. The scores of the

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homosexuals were significantly lower than those of a control group. A group of heterosexual neurotics, however, showed a similar deviation from the control group. The androgyny score, however, did not differentiate the homosexuals from the controls any better than did the biacromial diameter, which is less in these patients. It was concluded that homosexuals have a body-build similar to that found in patients with other psychiatric disorders and that it could not be specifically related to their sexual abnormality.

I thank Dr. P. D. Scott for permission to examine his patients, Dr. R. D. Hoare and Miss A Parker for taking the soft-tissue *x*-ray films, and Dr. H. S. Friend for arranging the examination of controls at Unilever House.

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DISTRIBUTION OF ANDROGYNY IN MENTAL PATIENTS

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The purpose of the present study is to investigate the physique of mental patients by using a measure of the relative maleness and femaleness of body build—the discriminant androgyny score (Tanner, 1951, 1955). Abnormalities in the psychosexual development of mental patients have been postulated and reported by many, and it is of interest to see if such abnormalities are reflected in the development of the corresponding physical endowment of these patients.

The androgyny score is a discriminant function from measurements of the bi-acromial and bi-iliac diameters of groups of normal men and women. The relative proportions of these two diameters have for many years been known to differ in males from those in females. The androgyny score enables the most effective differentiation to be made between the sexes using these measurements; the score is obtained as follows:

$$3 \times \text{bi-acromial} - 1 \times \text{bi-iliac diameter (cm.)}$$

Tanner found this score to have a normal distribution, with a mean and standard deviation of 90.1 and 4.7 for men and 78.9 and 4.6 for women. He found this score misclassified only 12% of the 409 men and women he examined.

The Investigation

Four groups of subjects of each sex were investigated. These were a control group, a group of schizophrenics, and a group with affective disorders; the last group was further divided into a group of patients suffering from a depressive illness and into a group suffering from various neurotic reactions. The male control group consisted of members of a large business organization. The female control group was obtained from an

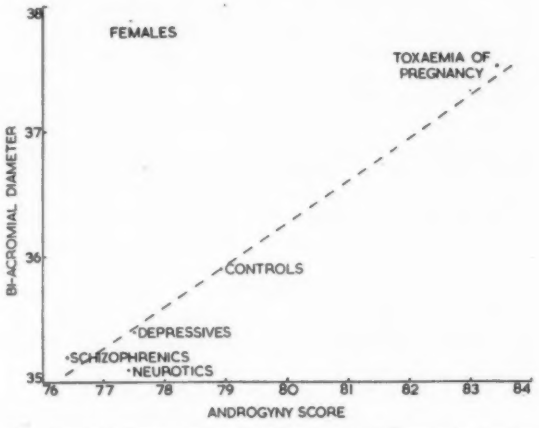

FIG. 1.—Androgyny scores and bi-acromial diameters in female patients.

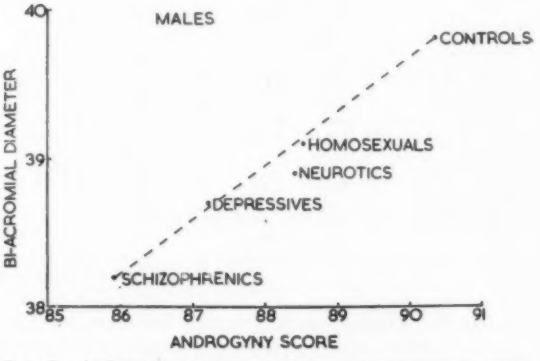

FIG. 2.—Androgyny scores and bi-acromial diameters in male patients.

antenatal clinic. None of the measurements used except weight are affected by pregnancy, and in each case the patient's earliest antenatal weight, recorded within the first months of pregnancy, was ascertained. The diagnostic criteria used followed those described by Mayer-Gross *et al.* (1954), with the exception that, for statistical purposes, depressive and neurotic patients were grouped together under the term "affective disorders."

The following measurements were made on each patient: weight, height, bi-acromial diameter, and

bi-iliac diameter. The last three measurements were all made by the same observer (A. J. C.), who used a Martin anthropometer. Patients were measured standing upright, shoulders relaxed.

Results

Tables I and II show the results and the statistical significance of the various measurements, and Figs. 1 and 2 show how the various groups are distributed with regard to the androgyny score and the bi-acromial diameter. A group of homosexuals in the males and a group suffering from toxaemia of pregnancy in the females are included as they have been compared with the same controls (Coppen, 1958, 1959). Except for the neurotic groups, there is little difference between the capacity of the androgyny score and that of the bi-acromial diameter to distinguish between various diagnostic groups. The androgyny score and the bi-acromial diameter are smaller in all the psychiatric groups (both sexes) than in the control groups. The female patients differ less from the controls than do the males, but the parallelism of the results in the two sexes is striking. Schizophrenics show a greater divergence from the controls than the affective (neurotic and depressive patients) group. The neurotics of both sexes differ from the controls, the schizophrenics, and the depressives because of their narrow bi-iliac diameter.

Discussion

The main difference between the groups is in the bi-acromial diameter, the bi-iliac differing only in the neurotics. Since the bi-iliac diameter is not significantly narrower from the controls in the other diagnostic groups, it follows that the bi-acromial differences are unlikely to be solely due to a general factor of narrowness, though such a general factor could play a part in the neurotics. Similar findings have been reported by other workers—for example, Rees and Eysenck (1945).

It has been shown that certain factors, such as height, age, and social class, may affect the bi-acromial and bi-iliac measurements, and data published by the Board of Trade (1957) give an indication of the extent of this interrelationship. Height varies slightly with age and social class. The bi-acromial diameter does not vary with age, but is slightly larger in subjects of the professional class. If the differences between the controls and patients were due to social-class factors one would expect to see this reflected in differences in stature between the groups; whereas the height of the groups does not show significant differences. Indeed, Clements and Pickett (1954) have shown that differences in chest girth between social classes disappear when standardized for a constant stature.

There is some evidence that the androgyny score or its most important component, the bi-acromial diameter, may be connected with certain other sexual and psychosexual characteristics. Thus Ferriman *et al.* (1957) found a significantly wider bi-acromial diameter in women with hirsuties and oligomenorrhoea than in controls. Lindegård (1956) reported a significant correlation between androgyny and size of penis.

TABLE I.—*Results in Control, Total Psychiatric, Schizophrenic, and Affective (Depressive and Neurotic) Groups. Comparison by "t" Test with Control Group*

	Controls		Total Psychiatric Group				Schizophrenic Group				Affective Group (Depression and Neurosis)			
	Mean	S.D.	Mean	S.D.	t	P	Mean	S.D.	t	P	Mean	S.D.	t	P
Males:	N=53		N=93				N=40				N=53			
Androgyny ..	90·3	4·1	86·8	5·8	3·9	0·001	85·9	6·1	4·1	0·001	87·8	5·6	2·5	0·02
B.A.D. (cm.) ..	39·8	1·6	38·5	2·0	4·3	0·001	38·2	1·8	4·3	0·001	38·8	2·4	2·5	0·02
B.I.D. (cm.) ..	29·3	1·3	28·9	1·4	2·0	0·05	29·0	1·6	1·9	0·1–0·05	28·8	1·3	2·5	0·02
Weight (kg.) ..	71·9	7·6	68·3	10·3	2·1	0·05	68·5	11·4	1·9	0·1–0·05	68·3	9·6	2·13	0·05
Height (cm.) ..	172·6	6·1	172·0	7·6	0·4	N.S.	170·8	6·8	1·3	N.S.	172·9	8·1	0·21	N.S.
Age (yr.) ..	41·5	10·5	3[illegible]·1	11·6	1·3	,,	38·6	11·6	1·2	,,	39 5	11·7	0·92	,,
Females:	N=50		N=138				N=46				N=92			
Androgyny ..	78·9	3·3	77·1	4·5	2·6	0·01	76·4	4·5	3·2	0·01	77·5	4·5	1·9	0·1–0·05
B.A.D. cm.) ..	35·9	1·2	35·3	1·4	2·7	0·01	35·2	1·6	2·4	0·02	35·3	1·3	2·7	0·01
B.I.D. (cm.) ..	28·9	1·6	28·5	1·5	1·5	N.S.	28·9	1·6	0	N.S.	28·2	1·5	2·5	0·02
Weight (kg.) ..	56·6	8·0	56·6	8·9	0	,,	62·2	10·3	3·1	0·01	53·8	8·2	1·97	N.S.
Height (cm.) ..	160·0	4·8	159·7	6·4	0·2	,,	159·2	7·0	0·6	N.S.	160·0	6·2	0	,,
Age (yr.)	24·1	4·1	38·6	11·5	8·7	0·001	36·1	11·0	7·3	0·001	39·8	11·8	9·29	0·001

B.A.D. = Bi-acromial diameter. B.I.D. = Bi-iliac diameter.

TABLE II.—*Affective Group Split into Depressive and Neurotic Groups. Comparison by "t" Test with Control Group*

	Depression				Neurosis			
	Mean	S.D.	t	P	Mean	S.D.	t	P
Males:	N=31				N=22			
Androgyny	87·4	6·1	2·48	0·02	88·4	4·8	1·74	0·1–0·05
B.A.D. (cm.)	38·7	2·5	2·37	0·05	38·9	1·9	2·26	0·05
B.I.D. (cm.)	28·9	1·6	1·22	N.S.	28·3	0·9	3·17	0·01
Weight (kg.)	69·1	10·1	1·43	,,	66·7	9·8	2·50	0·02
Height (cm.)	172·4	8·5	0·07	,,	173·6	6·7	0·70	N.S.
Age (yr.)	42·6	11·9	0·44	,,	35·1	11·8	2·37	0·05
Females:	N=63				N=29			
Androgyny	77·5	4·4	1·86	0·1–0·05	77·4	4·9	1·71	N.S.
B.A.D. (cm.)	35·4	0·4	1·67	0·1–0·05	35·1	1·2	2·93	0·01
B.I.D. (cm.)	28·6	1·6	1·00	N.S.	27·5	1·3	4·24	0·001
Weight (kg.)	54·2	7·5	1·71	0·1–0·05	52·9	9·8	1·90	0·1–0·05
Height (cm.)	159·8	6·0	1·06	N.S.	160·4	6·6	0·48	N.S.
Age (yr.)	43·9	12·7	12·40	0·001	31·0	9·8	4·37	0·001

B.A.D. = Bi-acromial diameter. B.I.D. = Bi-iliac diameter.

Raboch (1957) found that hypogonadal men, some with female sex chromatin, had a smaller bi-acromial diameter than normal controls. Coppen (1958) found a more masculine androgyny score in women with toxaemia of pregnancy. There is also some indication that the androgyny score or the bi-acromial diameter is related to psychosexual development. Raboch found in his group that libido was greatly reduced. Coppen found in his toxaemic group that not only was the female function of bearing children disturbed but that psychosexual difficulties were also often present in these women. Homosexuals have also been found to differ, with regard to androgyny and the bi-acromial diameter, from a control group (Coppen, 1959).

In order to offer a possible interpretation of our results a brief review of factors believed to play a part in sexual differentiation is necessary. Firstly, there is the genetic inheritance. Secondly, there is the differentiation of the internal and external organs of the sexual apparatus. Recent work (Jost, 1947, 1953; Segal and Nelson, 1957; Witschi *et al.*, 1957) has thrown a good deal of light on the subject. It takes place in two phases in mammals, at first *in utero* and later when development is completed at puberty. It is now known that in mammals the female type is the basic, neutral, non-hormonal type. In males masculinization takes place under the influence of foetal hormones. The absence of stimulation by the appropriate hormones at the exact time in the foetus leads to the female type of development. However, excessive androgenic stimulation at critical stages may lead to masculinization in the female. This state of affairs is the opposite of what is found in birds, where the "basic" type is male. The third aspect relates to the sensitivity of various parts of the body or receptors to differentiating hormones. This is greatest in the sexual and reproductive organs, but it appears that other parts of the body share this capacity to a greater or lesser extent. Vague (1956) has drawn attention to this factor.

Thus there are certain general somatic differences between the sexes, and two such body measurements—the bi-acromial and the bi-iliac diameter—have been found to offer a suitable index of such a general somatic sexual differentiation, though there are many others (see review by Tanner, 1955). This somatic difference between the sexes is present to some extent before puberty, but becomes very much more pronounced during and after puberty. The bi-acromial diameter shows the most marked sex difference; the bi-iliac diameter shows a moderate sex difference before puberty, but this difference decreases after this period.

Both male and female psychiatric patents have a narrower bi-acromial diameter, and it may be hypothesized that this is a result of a lack of development from the neutral type, which is basically female. This would account for the greatest abnormality appearing in male patients, for it is the male that travels furthest from the basic type, and thus abnormalities in this process of differentiation would show most in the male.

The point at which this abnormality appears is not known; it may be genetically determined or produced by environmental disturbances during the period of the child's growth. Ferriman *et al.* have shown the probability of a genetic inheritance in their group of women with hirsuties and an increased bi-acromial diameter. However, the psychologically disturbed parent will possibly affect the child's development both genetically and by providing a psychologically disturbing environment for the child to grow up in. Animal experiments with gentling—that is, stroking and petting—are of interest in this connexion. For example, Weininger (1954) showed that gentled rats grew larger and survived prolonged stress better than non-gentled rats.

Thus there may be several theoretically possible interpretations of these data, and further investigations of body build and its association with mental illness before and during puberty, together with genetic studies, are needed to clarify the problem.

Summary

The androgyny score, a measure of the relative maleness and femaleness of body build, was applied to the study of the physique of mental patients (schizophrenia, depression, and neurosis). Patients of both sexes had a significantly lower (more feminine) androgyny score and a narrower bi-acromial diameter than their control groups.

We are grateful to Dr. H. J. Friend for arranging the examination of the controls at Unilever House.

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The annual report of the Director of the World Health Organization Regional Office for Europe has recently been issued. This Regional Office, situated at Copenhagen, serves all the countries of Europe, with the exception of Hungary, Byelorussian S.S.R., and Ukrainian S.S.R., who do not at the moment actively participate in the work of W.H.O. The region also provisionally includes Turkey and Morocco at the request of their respective governments. The report describes the various health activities made available to member states at their request with the aim of improving health conditions in Europe. Besides traditional activities, such as the control of communicable diseases, important work has been undertaken to solve health problems particular to our times: air pollution, water pollution, the growing need to utilize surface waters in addition to the already well-exploited underground water resources of Europe, investigations into cardiovascular diseases, cancer control, and epidemiological research into various chronic and degenerative diseases. (*W.H.O. Report of the Regional Director*, July, 1958–June, 1959).

TRANSVESTITISM AND TRANS-SEXUALISM

A STUDY OF 50 CASES

BY

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Transvestitism is the impulse to wear the clothing of the opposite sex, and was given this name by Hirschfeld (1910). Ellis (1936) described the condition as a state of psychosexual inversion and called it eonism, after the Chevalier d'Eon, a French diplomat at the Court of St. James, who lived as a woman for much of his life. Trans-sexualism is the term used by Benjamin (1954) to describe the wish to change the anatomical sex. The nature of the condition suggests that transvestite and trans-sexualist individuals are predominantly homosexual in orientation and behaviour, and the following report on 50 such patients offers an opportunity to examine this possibility and the aetiological factors involved in the production of such deviate behaviour.

Norwood East (1949) stated that the desire to wear the clothes of the opposite sex was widespread. He did not indicate the frequency of its occurrence, but believed it to be more common than is realized. Transvestites proper were defined as those men who obtained sexual gratification from dressing as, and pretending to be, women; he found that in appearance, manner, and interest they appeared to be more feminine than masculine, but also remarked that some male homosexual prostitutes wear the clothes of the female sex to vary or enhance their attractiveness to men. The practice of cross-dressing is also found as a cultural variant in primitive societies; for example, Seward (1954) describes it as occurring among the Mohave Indians of North America, and also in the Iatmul people of New Guinea. Krafft-Ebing (1916) cites a report of similar behaviour found by Holder in the Montana Indians. The term transvestitism is not intended to include the wearing of the clothes of the opposite sex for theatrical purposes, burlesque, or disguise. In transvestitism the clothes or the wearing of them may provide an end in itself; they are usually endowed with sexual significance, and the act of wearing them may provide the sole form of sexual expression or outlet. The condition occurs in both sexes, though male patients come to notice more often as current fashions in female clothing permit transvestite women to wear garments which have male characteristics without undue attention being drawn to the transvestite act. Wearing the garments of the opposite sex is forbidden for both sexes by Mosaic Law (Deuteronomy xxii. 5).

Clinical Material.—The patients in the present survey comprise 37 males and 13 females. Many of these patients were referred from the endocrine clinic at Charing Cross Hospital, and were seeking operations "to change their sex" or advice on their problems.

Male Patients

Civil Status

Table I shows the civil status of the patients, and it will be seen that of 37 male patients 15 were married, two divorced, and four separated, so that 21 had achieved marital status. The preponderence of married over single men appears to indicate that the transvestite impulse cannot be equated in all cases with a lack of attraction to the female sex, and in these 21 men there had been adequate impulsion towards heterosexual

TABLE I.—*Civil Status*

	Transvestite		Trans-sexualist	
	Issue	No Issue	Issue	No Issue
	Males			
Married	7		5	3
Separated	1		2	1
Divorced			1	1
Single	1	7		8
	Females			
Married	1		1	
Separated			1	
Divorced				2
Widowed		1		
Single		2		5

relations in the male role, though two had married for "non-sexual" reasons. Four of the unmarried men lived an unusual variety of Lesbian relationship with older women. There was no heterosexual intimacy in these four cases; one of the patients living in this manner had achieved castration by a Continental surgeon.

Sexual Orientation

The sexual practices of the 21 married, separated, and divorced men varied from normal heterosexual relationships in the masculine role to homosexual fantasy; no married man had indulged in overt homosexual relationships, though this had occurred in 14 of the homosexually orientated males. Seventeen of the married, divorced, or separated men had fathered children.

Table II shows the sexual orientations of the 37 male patients assessed on the Kinsey scale of male sexual behaviour (Kinsey, Pomeroy, and Martin, 1948).

TABLE II.—*Sexual Orientation (Male Patients) on Kinsey Scale*

	Kinsey Rating						
	0	1	2	3	4	5	6
Transvestite	3	3	4	1	1	—	5
Trans-sexualist	—	2	9	4	—	—	5
Total	3	5	13	5	1		10

Fantasy and dream content were not taken into account in making these assessments; overt and admitted behaviour was considered a more reliable indication of actual sexual behaviour. Plichet (1955) had noticed selective memory in history-taking, and males requiring castration and change of sex frequently emphasize memories which indicate early feminine orientations to the exclusion of other more normal anamnestic content. These wish-fulfilling selected memories often form the basis of the demand for "sex-change." The possibility that latent homosexual trends might be present in any or all of the patients in this group is not excluded; many psycho-analytically orientated psychiatrists believe that such tendencies exist to some degree in all adults. Seven heterosexually orientated males wished to have castrating operations.

Table III shows the frequency and type of transvestite behaviour practised by these patients. Eight males were persistent and constant in their transvestite habits; they appeared habitually in women's clothes or in garments of such a type as to lead others to regard them as

female, and cosmetics were usually worn as part of the general assumption of female dress and appearance. Five men lived wholly as women and three others assumed a female role whenever this was possible. Eight men had appeared in public as female impersonators at some time in their history; four of these impersonators had been on the professional stage. The low incidence of professional female impersonators

TABLE III.—*Frequency and Type of Transvestite Behaviour*

	Males	Females
Persistent	8	5
Frequent	12	6
Occasional	6	2
Incidental to homosexuality	7	In all cases except 1
Partial transvestitism	4	

in the series suggests that such performers do not regard their behaviour as needing elucidation or treatment. On the other hand, many transvestites envy female impersonators the opportunity of appearing publicly as women. The four professional impersonators were, however, bored with the burlesque and deceptive aspects of their performances, preferring to be taken for veritable females; they all disliked the stage convention that the true sex should be revealed at the end of their performance. Twelve were less persistent in their cross-dressing but dressed as women as often as occasion permitted. Three men showed this behaviour very infrequently. In seven of the male patients (two psychopathic personalities and five homosexuals) transvestitism was an incidental and secondary manifestation. Partial transvestitism occurred in four male patients who for lack of opportunity wore only certain specific items of female attire, and in two other males a particular female garment appeared to constitute a true fetishistic object.

Occupations

Table IV shows the distribution of the cases into social class. There is a relatively higher incidence of the condition in the male professional group; one

TABLE IV.—*Occupations (According to the Registrar-General's Classification of Occupations)*

Social Class	Males	Females
I	2	—
II	8	—
III	8	6
IV	12	5
V	7	1
Unknown	—	1

medical practitioner, one member of the legal profession, two schoolmasters, and five professional engineers fell into this category. Four men had worked as waitresses, two being undetected in their impersonation; two others performed work normally undertaken by women; and three were in the employment undertaken by either sex.

Physical Characteristics

No case in the male series showed dysplasia of genitalia or major anatomical indication of femininity. Somatotyping was carried out in a number of patients, but gave no clear indication of female habitus or body build, though three had a very feminine facial appearance and were slightly built. The majority of the male patients were unmistakably masculine in appearance. Ketosteroid studies showed no abnormality, and buccal smears, where examined, showed male chromosomal structure.

Age at Onset

The onset of the transvestite impulse was almost always before the tenth year. The age at interview ranged from 16 to 50.

Personality Factors and Psychiatric Treatment

Table V shows the analysis of personality factors and psychiatric conditions occurring in the male transvestites and trans-sexualists. It will be seen that many of these

TABLE V.—*Personality and Psychiatric Assessments*

	Males	Females
Psychopathic personality	5	1
Obsessional ,,	11	2
,, neurosis	4	—
Homosexuality	12	9
Depressive state	1	1
Other	4	

patients showed obsessional personality traits; it was found repeatedly that compulsions to acquire and to wear women's clothes were present. Many patients reported a feeling of great contentment and relaxation when wearing female attire; some described the impulse as an omnipresent torture. In several cases the relatives of transvestites reported that the patients were kinder and more considerate when dressed as women. They enjoyed feminine tasks, helping their wives with cooking, housework, and other domestic tasks, or merely sitting around playing the feminine role. There was frequent assertion that a mistake had been made in the original attribution of sexuality, and this was justified by drawing attention to the (often assumed) feminine psychic orientations. In seven cases this psycho-sexual inversion was very marked. These ideas were held with obsessional strength, and, despite repeated explanation of the genetic, anatomical, and endocrinological basis of sexuality, such fixed ideas persisted, though their illogicality was accepted intellectually by the patients.

These obsessional personalities were preoccupied with thoughts of cross-dressing, of feminine activity, and fantasy of transvestite acts and opportunities. One man claimed that the desire to be female, and thoughts concerning transvestite behaviour, had seldom been out of his mind since the age of 8; several others made similar statements, commenting that these thoughts disappeared only when they were engaged in work requiring close attention. It was more common to find that the transvestite behaviour was phasic, and such variation of impulse is a common finding in obsessional states. Overt obsessional neurosis existed in four of these male patients, and three had been incapacitated by neurotic breakdown. A powerful desire to be seen in female clothing and the wish to be taken for a female were often present, despite obvious male sex and grotesque appearance. This indicates a strong exhibitionist tendency; and in fact only one man had not been seen by others when wearing female attire.

The trans-sexualist patients wished to assume the female role as completely as possible. They demanded castration and plastic surgery for the creation of female characteristics in the external genitalia, the formation of an artificial vagina, and mammoplasty. Two male patients have managed to secure this surgical intervention, and two others are awaiting such operations, having secured support for their view that they are so manifestly lacking in masculine traits, and so feminine in appearance, manner, and speech, that this step is

logical. A diagnosis of psychopathic personality was made in five cases; two of these patients had been in gaol; one was a psychopathic recidivist, and the other had been found guilty of importuning and masquerading as a woman. Others showed antisocial behaviour of serious degree in addition to the transvestite or trans-sexualist impulse. Three of these psychopathic individuals were practising homosexuals.

In two cases there was a family history of transvestitism unknown to the patients at the time of the onset of their own impulses. One man made an unsuccessful attempt at suicide, and one psychopathic patient committed suicide during a phase of severe anxiety and depression arising from hypochondriacal fears unrelated to his transvestite impulses. Four men had separated from their wives, and two had been divorced. The wives of two of the married trans-sexualist patients were willing to permit the castrating operation in order to please their husbands and to help them attain their desire. Several other wives accepted their husbands' contention that they were changing their sex and were willing to live with them on a sisterly basis. The attitude of the wives varied from abhorrence, perplexity, superstitious horror, and indifference, to sympathetic aid and understanding. Sympathy for the clinical condition as a personal problem was predominant, but such permissiveness provided opportunities for the exhibitionist tendency.

Female Patients

Thirteen female transvestites were seen; all had practised transvestitism and 10 wished to be masculinized. Their ages ranged from 20 to 44 years. Two were married, two had been divorced for desertion, one was a widow, and one other woman was separated from her husband. One of the married women frankly admitted that she married for security at the age of 44. One described her husband as effeminate. Two women had living children and another had miscarried. As in the male series, the onset of the transvestite impulse was early, usually before the age of 10 years. When children, their behaviour was tomboyish; they played with boys' toys, preferred boys' games, and often elected to wear shorts and jeans rather than dresses and other essentially female attire. There was no evidence of genital dysplasia or male anatomical conformation, but four women were quite masculine in appearance when wearing male dress and could be mistaken for men. Ten dressed their hair in short masculine style and wore clothing of severe masculine cut, or male garments having the male conventions for buttons, etc. Two dressed normally and attractively as females, one being an Indian woman who usually wore a sari.

Sexual Orientation.—With one notable exception, the female patients were homosexually orientated. These 12 women had experienced homosexual attachments, and the wish to take the male role in sexual intimacy with a Lesbian partner was the predominant and expressed reason advanced by those who wished for trans-sexualization. The sole heterosexually orientated woman was both transvestite and trans-sexualist; she presented the unusual pattern of heterosexual seduction by a male transvestite (not her husband). At first revolted by the deviate practices into which she was initiated, she became conditioned to experience orgasm in such acts, and attempted without success to secure her husband's co-operation in similar behaviour. Depression supervened and she made three unsuccessful attempts at suicide. She is an attractive woman and has one child.

Occupation.—Two of the females were dependent as wives; the remaining 10 were distributed almost equally between the unskilled, skilled, and clerical occupations. The social class of one was unknown.

Personality Factors and Psychiatric Assessments.—Two women had strongly obsessional personalities, and both had developed severe depressive illnesses with suicidal tendencies. Obsessional patterns also occurred in a woman tracer. The widowed patient presented as a case of anxiety state arising from frustrated Lesbian experience. Two other women appeared to be primarily psychopathic personalities.

Discussion

The psychological implication of these conditions have been assessed differently by various writers on the subject. In "Any Questions" in the *B.M.J.* of August 3, 1957 (p. 309), transvestitism was stated to have features of homosexuality, fetishism, and exhibitionism; it was suggested that transvestites were nearer psychosis than other perverts, and that some were, in fact, schizophrenics. This attitude had been advanced by Krafft-Ebing (1916), who considered that transvestitism was a state of transition towards paranoia sexualis. Wiedeman (1953) expressed the view that the castration impulse might be a symptom of an underlying schizophrenic process, and commented that transvestites presented the picture of an especially complex sexual deviation showing features of fetishism (over-evaluation of female clothing), homosexuality (desire to be a woman), exhibitionism (desire to show themselves as women), and masochism (as exemplified by the persistent desire for castration).

Fenichel (1945) suggests that the transvestite man supplants his love for the mother by identification with her and that the fetishistic components compel him to deny castration anxiety, so that the fetish represents the mother's penis, and he becomes the "penile woman." He explains the tendency to exhibitionism as the desire to demonstrate the symbolic penis and stated that narcissistic regression in these cases exceeded that found in homosexuality. In his view, female transvestites played a male role and wished to be identified with the father, having created the illusion that they had, in fact, a penis. East (1949) reports that the compulsive desire towards transvestitism might go as far as burglary and other crime in order to achieve the act. East considered that it was important to distinguish the transvestite from the homosexual, as transvestites often pass their lives showing no signs of sexual interest in their own sex. Peabody, Rowe, and Wall (1953) agree with East's definition of transvestitism and state that normal behaviour may include a lesser degree of this manifestation. They underline its relationship with fetishism, the fetish being regarded as the penis substitute.

Vague (1956) described three transvestites who were considered to have feminine endocrine and anatomical features. In only one of his cases does this view seem to be justified on the evidence quoted, as only one man had a body habitus approaching the female. Intersexuality is also advanced as a cause of transvestitism in a case reported by Gardien-Jourd'heuil and Gardien (1948).

Worden and Marsh (1955) failed to discover abnormal gonadal status in transvestite patients. They point out that the sense of being "male" or "female" is not a simple function of some biological endocrine or other factor, but is, on the contrary, a complex psycho-biological project. They believe that such patients are in conflict over strong but unacceptable sexual urges and feel threatened by all sexual activity, whether hetero-, homo-, or masturbatory. They regard such patients as shallow and immature and as having a grossly distorted concept of what a female is like socially, sexually, anatomically, and emotionally, and hold that for trans-sexualists the idea of castration represents an escape from sexual impulses rather than a wish for female sexual life. The transvestite, however, wishes to conserve the male organ. Ostow (1953) expresses an opinion very similar to this. Hamburger, Stürup, and Dahl-Iversen (1953) state that the terms transvestitism and eonism should be reserved for those men who have a rooted and irresistible feeling of being a woman. They believe that the condition is constitutionally determined and that some eonists are intersexes of the highest degree.

Plichet (1955) stresses the narcissism and the need for reassurance, affection, and approval found in these patients, and states that male transvestites wish to assume the favoured sexual position accorded to females in the modern world. He points out that the feminine identification is usually superficial, and comments that the desire of these patients for castration is incongruous with the psycho-analytical theories of fear of castration as an explanation for the condition.

Benjamin (1954), attributing the condition to infantile trauma, with fixations or arrested emotional development, postulated three types of transvestites: (1) Primarily psychogenic: anatomically male, they assume female identity and manner. (2) The intermediate type: the female appearance and orientation is often striking in these cases and they are regarded as psychic hermaphrodites, whose skeletal measurements may be eunuchoidal. (3) Somatopsychic transsexualism: these patients have a feminine appearance and orientation, with a greater degree of constitutional disturbance.

Vague (1956) describes the condition as an obsession and emphasizes the predominance of Lesbian behaviour in female cases. In rejecting psycho-analytical and other explanations he states that the cause is not known.

Conclusions

Certain constant features appear in the 50 cases reported above. In almost every case the onset of the transvestite or trans-sexualist wish was at an early age — usually before 12 years. There was a slight preponderance of married as opposed to unmarried men in the male series, and heterosexual relations occurred regularly in this group. The practice was found in all classes of men and women, though there seems to be a relatively higher occurrence among professional men. The majority of patients wished to wear the total clothing of the opposite sex, only four being partial transvestites. This suggests that transvestitism and transsexualism constitute a very complicated example of fetishistic behaviour, as partial transvestitism seems more akin to a simple fetish, in which a single item of clothing or other article is chosen as the fetish object. Almost all transvestites wish to appear in public in their assumed attire and to be accepted as a member of the adoptive sex. This tendency seems to be more pronounced among the male patients, and has an obvious relationship with exhibitionism. The craving for humiliation in female garb—in menial tasks or in subjection to a woman—indicates a masochistic trend in some male patients, and the demand for castration (or mastectomy in the females) echoes this masochism.

Two distinct groups of patient emerge.

1. The homosexual males and nearly all the female patients investigated; most of these patients demand transsexualization. This group appears to be primarily homosexual, and the transvestite urge a modification of the homosexual drive. These patients often rationalized their homosexual inclinations by claiming that they were undergoing physical metamorphosis which indicated a "change of sex." Such beliefs were found in patients of both sexes.

2. Obsessive-compulsive Group.—The impulse to wear the clothing of the opposite sex occurred as part of basic obsessional personality. This group was heterosexual in orientation; for such patients the clothes and the wearing of them provided the fetish object and aim for sexual satisfaction. These transvestite acts were often accompanied by, or were an adjunct to, heterosexual relationships. These individuals often experienced compulsions to practise and to fantasy transvestite behaviour; suffering, instead of gratification in the transvestite compulsion, is often experienced in these patients, who live the whole of their lives in the shadow of the impulse and in whom suicide may occur. Fernichel (1945) believes that "perverts" are compelled to like their perverted acts, whereas compulsive neurotics are tortured by their compulsions. There is little difference between these concepts, as both types of activity can be interpreted as manifestations of basic sexual drive. Despite the nature of this behaviour it appears that the desires of this group of males to wear female clothing is not identified with homosexual orientation.

No convincing evidence of anatomical intersexuality was found in any patient in the whole series. Thought disorder in the schizophrenic sense did not appear, and the occasional delusion of shrinkage of unwanted organs and change of stature appeared to be motivated interpretation and fantasy. The condition is to some extent associated with other forms of psychopathic behaviour. A characteristic attitude was the self-conscious assumption of idealized and wish-fulfilling concepts of masculinity or femininity, the subsequent use of this assumption to justify the practices, and the demand for surgical intervention, which is seldom, if ever, justified.

Summary

Current definitions of transvestitism and transsexualism are outlined, and reference is made to the occurrence of these conditions in different cultures. A group of 50 cases (37 male and 13 female) is described and analysed from the point of view of civil status, occupation, sexual activity, and psychic content. Their behaviour pattern is described and the absence of abnormal physical characteristics noted. Leading views in the literature are discussed. It is concluded that the case material reveals two predominant groups: (1) homosexual, and (2) obsessive-compulsive. The second group is found to be proportionately larger among the male patients. It appears that homosexuality is not necessarily present in every case of transvestitism.

Acknowledgments are due to Dr. Joseph Adler, clinical assistant, Endocrine Clinic, Charing Cross Hospital, for assessments of the physical status of many of these cases.

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DISTURBANCE OF MOTOR FUNCTION DURING TREATMENT WITH IMIPRAMINE

BY

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Imipramine hydrochloride ("tofranil"; N-γ-dimethyl-aminopropyl-iminodibenzyl hydrochloride) has recently been introduced into psychiatric practice. We have been using it for treatment of depressive illnesses and have observed some beneficial results. Some patients, however, have suffered side-effects of such a nature as to preclude further administration of the drug. It has been stated that side-effects are of minor consequence (Kuhn, 1958; Azima, 1959). It is our purpose to draw attention to other side-effects which have led to undesirable consequences even when patients have been under close supervision in hospital.

It would appear that incoordination of motor activity may be produced by the drug when used in therapeutic dosage. In our cases this has presented as falling, dysarthria, and coarse tremor. This may well be a manifestation of the dystonic type of motor disturbance already described by us (Lancaster and Foster, 1959) for imipramine and by Montgomery and Sutherland (1959) for perphenazine.

The following case reports are illustrative of these disturbances. The patients are predominantly female, as we personally deal largely with female patients.

Case Reports

Case 1: Endogenous Depression.—This patient, a woman aged 72, was the one responsible for drawing our attention to this type of symptom. She suffers from recurrent depressive episodes, and had previously been treated by electric convulsion therapy (E.C.T.) with much benefit. In this episode it was decided to give imipramine, and a course was begun, starting with 25 mg. b.d. and increasing by 25 mg. a day to 75 mg. t.d.s. After a few days she was reported to have fallen several times. She said that she "fell backwards" and, indeed, was observed to do just that. She would take several paces backwards and then fall down. One was reminded of the retropulsion of Parkinsonism. No rigidity or other signs to suggest this were found. Fortunately, although she fell down several times, she escaped injury other than bruising. She also complained of the previously described side-effects of dryness of the mouth, sweating, and constipation. She denied that there was any feeling of faintness, giddiness, or dizziness which might have suggested hypotension, and no alteration in the blood-pressure was observed. The drug was stopped in view of this disturbance and E.C.T. was given instead. There were no further episodes of falling, and she made an excellent recovery.

Case 2.—This woman, aged 69, was under treatment for endogenous depression—the fourth occasion since 1951. She also was observed by the nursing staff to "fall backwards." The patient described this as "losing my balance and going down backwards." It happened on several occasions. On one occasion she was staring rather vacantly out of the window, suddenly lost her balance, and fell over backwards. This patient is of special importance in this connexion, since while this paper has been in preparation she has continued to have imipramine 50 mg. t.d.s. Unfortunately, she has fallen again, and this time has suffered a fracture of the neck of the right femur.

Case 3.—A woman aged 55, with involutional depression. She was given imipramine to 50 mg. t.d.s. Two days later she complained bitterly of "pins and needles" in the arms and legs and of a dry mouth. A gross tremor of the hands and feet occurred, without rigidity. She slipped and fell on the fourth day of treatment and has to hold the bannister rail. She feels tottery, but denies any feelings of faintness or giddiness.

Case 4.—A woman aged 72, with endogenous depression. She is a diabetic, and has been a resident in the hospital for two years. She has poor eyesight, with a cataract in the right eye. She tends to become recurrently depressed and has been treated by modified E.C.T. This time imipramine was given in small doses—25 mg. t.d.s. Four days later she fell in the ward and suffered a fracture of the neck of the right femur.

Case 5.—A woman aged 72, with endogenous depression. Previously she had been treated with modified E.C.T. She relapsed within two months of leaving hospital in December, 1958. Treatment with imipramine was carried to quite high dosage and then reduced to 25 mg. t.d.s. She became a little brighter and less depressed, but E.C.T. was given subsequently. She developed a slurring dysarthria and a grossly ataxic gait, so that she had to be constantly attended by the nursing staff. Imipramine was withdrawn and the dysarthria and ataxia cleared up. Modified E.C.T. was continued and a good recovery made. Social factors are solely responsible for her further stay in hospital.

Case 6.—A woman aged 56, with endogenous depression. A long-stay patient living in the same villa for years. Imipramine was given for a depressive episode. She fell twice during treatment—bruises and abrasions only. The first time she slipped and fell while out walking. The second time she described how, while going upstairs, she felt paralysed, felt she had no control over her legs, and fell downstairs; she felt weak and shaky and her face began to sweat. She did not faint, however, and when seen by the nursing staff within a few moments was fully conscious.

Case 7.—A woman aged 47, with endogenous depression. An acute depressive illness. Given imipramine. Describes how she felt "giddy and faint" and fell "sideways on to the grass."

Case 8.—A man aged 49, a case of endogenous depression. He fell while in the "toilet" and suffered a fractured ankle while receiving imipramine in doses of 50, 50, and 75 mg. a day.

Case 9.—A woman aged 54, with involutional depression. Was treated once by modified E.C.T., then relapsed.

Imipramine given, as she refused further E.C.T. At one period she developed a coarse tremor of the limbs so that she dropped objects from her hands. She recovered from this disability when the dose of imipramine was reduced. In her case E.C.T. was also required.

Discussion

During the period covered there were no other fractures in the hospital, and the only other falls recorded in the ward casualty books were during three epileptic attacks. It should be emphasized that falls in a mental hospital may possibly be of considerable legal import and that the records are most carefully kept.

Although the cause of falling in these patients is difficult of proof, a reasonable case can be made for regarding the ones described as due directly to the ingestion of the drug.

Thus:—(1) None of the patients had previously fallen or shown any evidence of motor difficulties or instability. (2) Clinical examination had been uniformly normal. (3) Side-effects, already known to be attributable to the drug, were present. (4) All disturbances disappeared on withdrawal of the drug. (5) There was no unconsciousness, no "black out," and no clinical signs suggesting syncope or epilepsy. (6) One patient (described elsewhere) who ingested 1,500 mg. of imipramine in a "suicidal attempt" suffered from uncontrollable movements of the limbs of a dystonic nature, but not from syncope. (7) Minor falls of blood-pressure have been observed, especially in hypertensive patients. No actual hypotensive syncopal attacks have been seen. (8) The dosage of imipramine did not exceed that recommended by the makers for routine therapeutic administration.

We think that it is therefore possible to say that imipramine may produce disturbance of motor functions, in addition to any hypotensive effect that may be present; also, that from this aspect there are considerable individual differences in tolerance to the drug. In most cases these side-effects are of minor importance, but it should be borne in mind that in some they may lead to serious injury. This would appear to be more probable in the elderly. These observations confirm those made by English (1959), and may represent a serious limitation to the use of the drug.

It should be pointed out that no clinical trials have yet been published in this country and also that early reports can be regarded as no more than encouraging. We would therefore, for the present, advise caution in its use. There is little evidence so far that imipramine can replace E.C.T., which in its modified form has proved extremely safe and effective. Extensive trials will be necessary before the drug can be unreservedly recommended. In the meantime E.C.T. remains the treatment of choice for the severely depressed patient.

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During the 12 months covered by the Family Planning Association's *Annual Report, 1958–9*, 340,000 people attended F.P.A. clinics, 20 new clinics were set up, making a total of 292, run by 242 branches, and at headquarters, on a conservative estimate, there were over 21,000 requests for advice and F.P.A. services.

C

INFECTIVITY OF THE PRIMARY TUBERCULOUS COMPLEX

SOME COMPLICATIONS IN CHILDHOOD

BY

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Recent advances in methods of detection, prevention, and treatment of adult tuberculosis have lowered the incidence of infection and disease in childhood to such an extent that the demand for hospital accommodation for infected children has been greatly reduced. Most paediatric physicians in the British Isles are prepared to treat such children in open children's wards without isolation, but there are those, particularly in the Scandinavian countries, who believe this to be wrong and who regard childhood tuberculosis as potentially infective.

A survey was therefore carried out at the Lissue Branch Hospital of the Royal Belfast Hospital for Sick Children in 1953 and 1954 in an attempt to assess this risk. Out of a total of 374 admissions there were 103 actively tuberculous children. Of these, 72 had simple or complicated hilar adenitis, six had pleural effusions, and one had post-primary pulmonary tuberculosis. There were 13 children with cervical adenitis, five with bone and joint disease, two with mesenteric adenitis, and one each with lupus vulgaris, mastoiditis, chest-wall abscess, and pericarditis. Routine gastric lavages were not carried out on all these children, and only one was given antituberculous chemotherapy (the child with the suspected post-primary disease). The average duration of stay for the whole group was 85 days. Sixty-three children were tuberculin-positive and were presumed to be inactive—48 following natural infection and 15 following B.C.G. vaccination.

Method of Tuberculin-Testing

On admission to the Branch Hospital a diagnostic tuberculin jelly test was applied, irrespective of the tests carried out in the main hospital. This was read as positive or negative in most cases and as doubtful in a few. When the result was doubtful the jelly test was followed by a Mantoux 1/1,000; 10 tuberculin units.

Since the time that this survey was carried out there has been increasing criticism of the efficiency of the tuberculin jelly test. We were aware, even at that time, of the disadvantages of the test, and we therefore took great care in its interpretation. We limited the follow-up tuberculin test to the diagnostic jelly test when we thought the usual criticism of the reading of the test did not apply, as in each case it was clearly negative. This criticism almost always applies to the danger of false-positive results—that is, reaction to the strapping rather than to the tuberculin in the jelly. We feel also that the diagnostic jelly test was sensitive enough for our purpose, because if the individual had developed a primary complex he or she would have reacted quite strongly.

In those cases where the original test was negative, and in all the cases negative to Mantoux 1/1,000, a

Mantoux 1/100 (100 T.U.) was carried out. This means that a child was not considered tuberculin-negative until there was no reaction to 100 T.U. at the end of 72 hours. Thereafter on all tuberculin-negative children a diagnostic jelly test was performed during the first week of every month that the child was in the Branch Hospital. After discharge the patient was recalled to the out-patient department for a further jelly test in six to twelve weeks (occasionally a little later).

Results of the Survey

Of the 209 children who were tuberculin-negative at the beginning it was found possible to follow up 177, and at no time during the period of observation within the hospital or after discharge did any single child develop a tuberculin-positive reaction. It was found impossible to recall 16 other children for their tests after discharge. In order to complete the survey it was necessary to fix a closing date, and at that time there were still nine children in hospital whose average stay was considerably in excess, even at this time, of all other children in the group. Five other children had B.C.G. vaccination during the period under observation. Two children died—one from congestive heart failure following rheumatic carditis and the other after operation for a congenital heart lesion. The average duration of stay in hospital for this group was 58 days.

Discussion

Rarely a child with a primary tuberculous complex might suddenly and without warning develop a post-primary pulmonary lesion which would rapidly become infective and therefore dangerous. Experience both in and out of hospital has shown that this is an extremely uncommon complication, but nevertheless one which does occur on occasion. It was therefore thought wise to have a monthly *x*-ray examination on each child while in hospital.

Another aspect of the possible spread of tuberculosis in these circumstances is the mobility of the children while in hospital. It was the custom to confine most of them to bed for an initial period of variable duration and to allow more freedom of movement for a longer time each day as they improved Eventually they were permitted to attend the school in the classroom. Even if the child with tuberculosis was kept relatively isolated in bed, other children suffering from other conditions were given complete freedom of movement in the hospital so that they very often played with the tuberculous children We feel that in the circumstances the possibility of other children becoming infected would have been high if the children with tuberculosis were infective, but the results have shown that cross-infection did not seem to occur. The one child with a post-primary pulmonary lesion was kept under very close radiographic supervision, and the response to chemotherapy was so rapid that it seems likely that the infectivity of this particular lesion was extremely low or even non-existent. Eight gastric washings were done at regular intervals, and all proved negative on culture.

The low infectivity of childhood pulmonary tuberculosis is probably due to the small size of the primary foci, to their rapid healing, and to the child's habit of swallowing rather than spitting out his sputum.

Experience has also shown that when one child in a family develops a primary complex from an infection outside the home then it is rare for other children in the same family to develop the disease unless they have been in contact with the original case.

There is, however, another extremely important aspect to the nursing of primary tuberculosis in an open children's ward. It is that the source of infection must be found as quickly as possible, particularly if the infecting individual is likely to be visiting the child. On such visits people tend also to pay attention to other children and might well infect them. In other words, the danger lies not with the child as a patient but with the adults or adolescents coming to see him. It therefore was the practice to ask the parents wishing to visit the children not to do so until a clear chest *x*-ray picture was available. This was arranged on the night of the admission of the child so that parents could be allowed to visit from the following day provided that their chest *x*-ray films were normal. It was also requested that the other relatives would not visit them unless they had normal chest films.

Summary

Of 374 children admitted to hospital, 209 were tuberculin-negative. Of the latter 177 were tuberculin-tested after discharge.

These children were nursed in normal association with cases of childhood tuberculosis, and it was found that six or more weeks after discharge 177 were still tuberculin-negative—that is, there was no evidence that they had developed primary tuberculosis while in hospital.

The danger of nursing tuberculous children among other children arises not from the child as a patient but from the adults who may visit the child.

Chest radiography of these adults should be carried out with a minimum loss of time so that visiting to the child is not interfered with.

We are indebted to Professor F. M. B. Allen and the members of the medical staff of the Royal Belfast Hospital for Sick Children for allowing us access to their cases, and to Dr. F. J. W. Miller for much helpful criticism and advice.

FOOD AND INDIGESTION

AN INVESTIGATION OF POSSIBLE RELATIONSHIPS

BY

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I am convinced digestion is the great secret of life.—
SYDNEY SMITH, 1837.

Many people who have no disease of the gastro-intestinal tract find that certain foods disagree with them. Such foods are said to be "indigestible" in the sense that the process of digestion involves discomfort and untoward symptoms. Alvarez and Hinshaw (1935) studied 500 patients and suggested several likely mechanisms whereby foods might disagree with people. The response of the gastric acidity to food has been extensively studied by Rehfuss and his colleagues (Bergeim *et al.*, 1919; Fishback *et al.*, 1919a, 1919b; Smith *et al.*, 1919; Miller *et al.*, 1919, 1920a, 1920b, 1920c, 1920d), and the gastric emptying-time after various foods by Wilson *et al.* (1929) and Maile and Scott (1935). However, as the *Lancet* (1935) pointed out, "It is strange how little relation gastric acidity and gastric emptying often bear to actual digestibility of foods, as evidenced by symptoms of 'indigestion' or their absence."

Very little experimental work has been published correlating symptoms of indigestion with the possible mechanisms causing them. Brummer and Bundul (1950) studied radiologically 36 dyspeptic patients who had been given food mixed with barium; 12 developed pain. They concluded that the type of food did not influence their results and found no relationship between epigastric pain and gastric or duodenal motility. Brummer and Sysimetsä (1957), using similar methods, found a short-lived decrease in gastric motility in dyspeptic patients after drinking black coffee with cream, which normally caused indigestion. It was not stated, however, whether the patients had symptoms during the tests.

It was decided to study some of the possible organic factors which might be involved in indigestion due to specific foodstuffs, particularly the presence of gastro-oesophageal reflux, alterations in gastric motility and acidity, time of transit through the small intestine, distension of the gastro-intestinal tract by masses of food or air, and impairment of gall-bladder function. Correlation of these functions with symptoms at the time of the test would then be made.

Material and Methods

Dyspeptic patients in whom a barium-meal examination revealed nothing abnormal were studied. Peptic-ulcer patients were avoided because of the complicating factor that the cause of ulcer pain is unknown. For a similar reason patients with a history suggestive of peptic ulcer were excluded, even in the presence of a normal result of the barium-meal examination. All patients who were selected thought that there was a definite relation between their dyspeptic symptoms and the type of food eaten. A detailed dietary history was taken from 70 such patients (37 males and 33 females) whose mean age was 42.9 years (range 18–66), and the following examinations were made on 36 volunteers (19 males and 17 females) from this group. Six ounces (170 g.) of the indigestible food, the nature of which varied with the individual patient, together with ½ oz. (15.5 g.) of barium sulphate ("micropaque" in 13 patients and "microtrast" in the remainder) were eaten by the patient, who had fasted overnight. The gall-bladder was outlined by six iopanoic acid tablets taken 12 hours previously.

After the patient had been screened and one *x*-ray film had been taken, the meal was eaten and further films were taken after five minutes, 30 minutes, one hour, two hours, and three hours. In six patients barium sulphate was not given until two hours after the food had been eaten. If the stomach appeared empty at three hours, 4½ oz. (128 ml.) of diluted barium sulphate solution was given to ensure that the food had not separated from the original barium sulphate and remained behind in the stomach.

In 21 patients gastric acidity was studied at the same time, a radio-opaque Levin tube being passed through the nose into the stomach at the onset of the test before the meal was eaten. The tube was adjusted during the preliminary screening so that the samples of gastric juice obtained came from the body of the stomach: 5-ml. samples of gastric contents were aspirated at 15-minute intervals for three hours.

Between *x*-ray examinations the patient lay propped up on a couch. In six patients the effect of exercise was assessed, the patients walking up 80 steps and back immediately, one hour, and two hours after the meal.

The test was subsequently repeated a few days later in the same patient under similar conditions, except that 6 oz. (170 g.) of a control food which did not normally cause dyspeptic symptoms was eaten by the patient. During each test gastro-oesophageal reflux was looked for 30 minutes after food. The emptying of the stomach was estimated by measuring the area of the radio-opaque surface of the *x*-ray film at various intervals of time, using squared graph tracing paper, and expressing the results as a percentage of the initial opaque area. Similar measurements were made to estimate gall-bladder contraction. All the films were taken in the erect postero-anterior position. The *p*H of the gastric contents was measured, using the Cambridge *p*H meter and the sealed glass electrode: the free and total acid in the filtered gastric samples were measured by titrating with N/10 NaOH, using Töpfer's indicator. Preliminary experiments showed that the presence of barium sulphate did not affect the measurement of gastric acidity by these methods.

Dietary Survey

Table I shows the foods that disagreed with 15% or more of the 70 patients. It will be seen that many of the foods have a reputation for being indigestible.

TABLE I.—*Foods Which Commonly Disagree with "X-ray-negative" Dyspeptics*

Food	% of Patients with Symptoms*	Food	% of Patients with Symptoms*
Fried foods	52†	Sardines, New brown bread, Spring onions, Bananas	18
Pastry	33	Raw cheese, Kippers, Roast potatoes, Pineapple, Plums, Baked beans	17
Cucumber	33	Haddock, Thick soup, New white bread, Chocolates, Bacon, Lettuce	15
Pickles, Apples	30		
Spices, Cooked cheese	27		
Oranges	26		
Sausages, Suet puddings, Curry	24		
Radishes, Onions, Nuts	23		
Pork	21		

* Excluding "repeating of food," as is frequent with onions, radishes.
† A further 23% of patients avoided fried foods.

These figures do not include patients who said they avoided certain foods in case these caused indigestion. Thus a further 23% avoided fried foods for this reason.

Experimental Administration of Indigestible Foods

Twenty-one different types of indigestible food were given to the 36 patients (Table II). Only five had dyspeptic symptoms during or after the test, and as one of these also had symptoms with the control food she can be excluded (Table III). Of the remaining four patients gastro-oesophageal reflux was present in two, one of whom was also found to have a sliding hiatus hernia. Reflux did not occur during any of the other

TABLE II.—*Types of Indigestible Foods Administered to 36 Patients*

Food	No. of Patients	Food	No. of Patients
Fried fish and chips	4*	Boiled fish	1*
,, sausages	1	Twice-cooked meat	1
,, egg, sausages, and bread	1	New bread	2
,, ,, bacon, and bread	5*	Jam tarts	1
,, ,, ,, ,, tomato	3*	Lettuce	1
,, ,, ,, ,, chips	1	Bananas	2
,, mushrooms on toast	1	Apples	3
Cheese	1	Oranges	1
Cheese sandwich	1	Melon	1
Welsh rarebit	3*	Pineapple	1
Sardines	1		

* Dyspeptic symptoms occurred in one patient in this group.

examinations. The other two patients had pain after eating fried food and are considered in more detail later.

Three more patients had dyspeptic symptoms after eating the control food only, and no symptoms after the indigestible food. Aerophagy with subsequent

TABLE III.—*Results of Food Tests*

Total No. of patients tested	36
No. having pain on eating indigestible food only	4*
" " " " " " and control food	1
" " " " " control food only	3

* 2 of these patients were shown to have gastro-oesophageal reflux.

distension of the gastro-intestinal tract was surprisingly infrequent, and was never associated with symptoms other than belching. There was no intestinal distension with large opaque masses of food, nor was there any evidence that the food and barium became separated in the stomach. Intestinal hurry was not present during any of the examinations.

The emptying-times of the stomach were within the expected limits for all patients. Thus after meals, consisting mainly of carbohydrate, the stomach was empty in three hours in every case; in contrast, emptying was incomplete at three hours in all the patients who ate fried foods. The level of gastric acidity again varied with different foods, but there was much overlap. It was usually less for the first two hours after fried foods than after non-fatty foods, while carbohydrate foods had only a short-lived stimulating effect. The shapes of the curves obtained by estimating *p*H and titrating free acid were similar, but it is likely that when food is present the former gives a more reliable estimate (James and Pickering, 1949). In every case the gall-bladder concentrated the dye satisfactorily and contracted after suitable food, though not of course after carbohydrates.

The two patients who had symptoms without gastro-oesophageal reflux after eating the indigestible food are dealt with below.

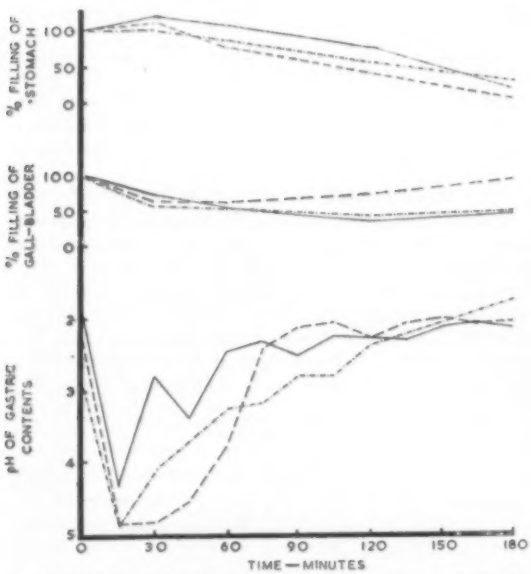

FIG. 1.—Effect of fried food on gastric emptying, gall-bladder contraction, and gastric *p*H in Case 1, compared with a control food and with fried food in eight symptomless patients. In the bottom graph the mean curve after fried food is of four patients only. ——: Case 1, after fried food. - - - -: Case 1, after control food. —·—·—: Mean curve after fried food, eight patients.

Case 1

A man aged 44 said that whenever he ate fried food he developed a burning epigastric pain soon afterwards. Half an hour after eating the test meal of fried egg, bacon, bread, and barium he complained of this pain, which lasted two and a quarter hours. In contrast he had no symptoms after eating the control meal of scrambled egg on toast with barium 12 days later.

It will be seen from Fig. 1 that the *p*H of the gastric contents was greater than two after the meal, and after the first hour was very similar to that of the control meal. It was also of a similar order to the mean curve of four patients who ate the same food without getting symptoms. The rate of stomach-emptying was slower after fried food (stomach 16% full at three hours) than after the control food (stomach empty at three hours): this would be expected in view of the higher content of fat of the fried food. There was less difference compared with the mean emptying-time of eight patients who ate fried food without symptoms (stomach 27% full at three hours).

There was a close correlation between contraction of the patient's gall-bladder after fried food and the mean curve of the eight symptomless patients. The control meal caused less-sustained contraction, in keeping with the smaller fat content. Thus this patient's symptoms after eating fried food were not related apparently to the gastric and gall-bladder functions that were measured.

Case 2

A woman aged 58 complained of attacks of right-sided abdominal pain usually after meals and invariably brought on by fried foods. Twenty minutes after the test meal of fried egg, bacon, tomato, and barium she complained of this pain, which lasted one and a half hours. There was no pain after eating the control meal of poached egg on toast with barium.

No studies of gastric acidity were made. Stomach-emptying after the fried food was similar to that after the control meal (Fig. 2). Comparison with the curve of the mean emptying-time of the eight symptomless patients

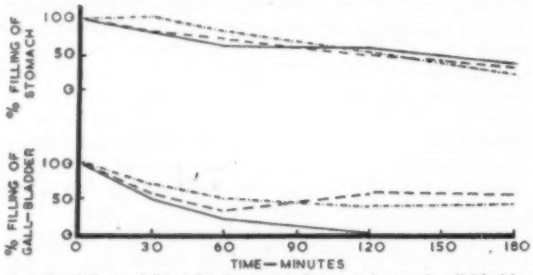

FIG. 2.—Effect of fried food on gastric emptying and gall-bladder contraction in Case 2, compared with a control food and with fried food in eight symptomless patients. ——: Case 2, after fried food. - - - -: Case 2, after control food. —·—·—: Mean curve after fried food, eight patients.

again showed close similarity. Gall-bladder emptying was more rapid and complete in the patient after the fried food than after the control food, and was comparable to the mean curve of the eight patients. There was no *x*-ray evidence of associated dilatation of the common bile-duct which would suggest spasm of the sphincter of Oddi at the time of gall-bladder contraction, so it seems unlikely that the pain was related to the contraction of the gall-bladder.

Discussion

It is clear from these results that in spite of the belief of all the patients studied that certain specific foods brought on their symptoms, this effect occurred in only four out of the 36 patients when some of these foods were tested, and gastro-oesophageal reflux was present in two of these, and may be presumed to account for their symptoms. In the other two patients no

mechanism for their pain was demonstrated. This does not necessarily mean that the symptoms have a psychological basis, but they may well be due to the inadequacy of the methods used to detect abnormal functioning of the gastro-intestinal tract. However, the occurrence of pain in one patient with both the control and the indigestible foods, and in three others with the control food alone, suggests that the actual composition of the food is not responsible for these patients' indigestion.

These results are surprising. Foods have long been held to be a cause of dyspeptic symptoms. Brinton (1864) suggested a classification of dyspepsia "according to that alimentary constituent, the failure of which to be digested provokes their symptoms." Alvarez and Hinshaw (1935) considered as possible causes of distress after the eating of certain foods, allergy, drug-like substances in the food causing bowel irritation and altered gastro-intestinal peristalsis, and the bulk effect of cellulose-containing foods. They pointed out that a food which is tasted during belching or regurgitation, such as onions, is more likely to be blamed than one which is not: accordingly, such foods were not used in the present tests, though this is unlikely to be the explanation of the failure of nearly all the patients to get symptoms.

Previous workers have shown that various foodstuffs can alter gastric motility. Thus Wirts *et al.* (1954) showed that tea appeared to stimulate gastric motility and increase the rate of emptying compared with water. Brummer and Sysimetsä (1957) compared the effect of black coffee and black coffee with cream on gastric motility, studied radiologically in dyspeptic patients and controls. Most of the dyspeptic patients showed an immediate, short-lived decrease in gastric motility after coffee with cream, not seen with the control patients. No mention was made of correlation of these findings with symptoms, but in any case the authors felt that these were not the cause of the dyspeptic symptoms. Siurala *et al.* (1953) studied 130 *x*-ray-negative dyspeptic and 56 non-dyspeptic patients, but were unable to find any relationship between *x*-ray changes in the stomach and acid secretion and the patients' discomfort. However, they felt that their methods were inadequate to rule out functional disorders of the stomach as a cause of distress related to meals.

The present results are in agreement with those of Brummer and Bundul (1950) previously mentioned, though a third of their patients developed pain during the tests with indigestible foods. The patients in the present series were selected because they were subject to dyspepsia and were certain that this occurred after some but not all foods. Thus a bias would be expected in favour of their developing symptoms. It might be thought that, as with ulcer pain induced by the administration of intragastric hydrochloric acid, symptoms could be reproduced only during an active bout of dyspepsia. But the dyspeptic symptoms attributed to specific foods by these patients were said to occur whenever these foods were eaten and were not cyclical, as is usual with ulcer patients.

It is possible that the abnormal experimental conditions, such as the eating of food mixed with barium in unusual surroundings or the presence of a stomach-tube in some patients, might invalidate the results: but these conditions would be expected to accentuate rather than diminish symptoms, particularly if these were psychological in origin. That the stomach-tube plays a part is unlikely, as symptoms occurred in two patients with a tube and two without. Further confirmatory evidence that the failure to produce symptoms was not due to experimental conditions comes from 14 of the patients who subsequently ate the indigestible food at home without symptoms. It might also be argued that patients forget after a time which foods do in fact upset them. However, symptoms had been present in 10 of the patients for less than two years, but only one of these had symptoms during the test.

In case barium sulphate made the food more digestible the barium was not given until two hours after food in six patients, none of whom developed symptoms. The amount of food eaten might affect the incidence of symptoms, but this was standardized and corresponded so far as was possible to an amount normally eaten, such as a fried egg, two rashers of bacon, and one slice of fried bread. Speed of eating might be another factor, but is unfortunately subjective. Eighteen patients said they ate quicker than average, 10 slower, and only eight at average speed. Two of the patients with symptoms fell in the quick group, and two in the average group. It seems unlikely, therefore, that this plays a significant part in the production of their symptoms. Mixtures of food rather than single foods might be the cause of indigestion attributed to a particular food, but this would be an extremely difficult hypothesis to test.

Sitting down for three hours after a meal is another possible explanation for the failure of the patients to develop indigestion, but only one of the six patients who were exercised after a meal developed symptoms. In the two patients who developed symptoms which have not been explained there was no evidence of allergy. Neither was this a likely explanation for the symptoms complained of by the patients: a personal or family history of allergic disorders was given by only four of the patients, none of whom developed dyspeptic symptoms during the tests.

The most likely explanation is that in these patients with non-ulcer dyspepsia the actual nature of the food is not an important factor in the production of their dyspeptic symptoms. There are so many well-known indigestible foods that almost any bout of indigestion, whatever the cause, is likely to have been preceded by the eating of one of these foods during the previous few days. This particular food is then wrongly held responsible by the patient for the symptoms. Perhaps Mark Twain gave good advice when he said that the secret of success in life is to eat whatever you like and let the food fight it out inside.

Summary

A dietary survey of 70 patients with non-ulcer dyspepsia who attributed dyspeptic symptoms to certain specific foods was made. Thirty-six of these ate an "indigestible" food mixed with barium sulphate and were radiographed at intervals for three hours: the gall-bladders of these patients were outlined with iopanoic acid. Simultaneous studies of gastric acidity were also made in 21. The studies were subsequently repeated, a non-indigestible food being used as a control.

An attempt was made to correlate the patients' symptoms during the tests with the findings from these investigations. Only four patients developed symptoms with the indigestible food: gastro-oesophageal reflux was present in two, but no mechanism was apparent in the other two. One other patient had symptoms with both the indigestible and the control food, and three with the control food alone.

It is concluded that in these patients the composition of the food did not play an important part in the causation of their dyspeptic symptoms.

My thanks are due to Dr. H. L. Marriott for his encouragement and advice; to the physicians of the Middlesex Hospital for permission to study patients under their care; to Mrs. M. Fyfe for technical help; to Miss E. Wilkinson Hughes, senior dietitian, the Middlesex Hospital; and to Mr. T. E. Cowan for Figs. 1 and 2.

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Medical Memoranda

Suicidal Attempt by Imipramine Overdosage

Imipramine ("tofranil") is an iminodibenzyl derivative which has recently been introduced for the treatment of depressive states. While its value in these conditions is still under investigation there have been reports of some side effects, and these include dryness of the mouth, giddiness, tachycardia, disturbances of accommodation, fine tremor, and hypotension (Kuhn, 1957; Kielholz and Battegay, 1958). There has been only one report (Moll, 1959) of the effects following the ingestion of a large quantity, and accordingly it may be of interest to record the following case.

CASE REPORT

A woman aged 29, a trained nurse, suffering from a recurrent depressive illness and previously treated with electric convulsion therapy, had been taking imipramine, 25 mg. t.d.s., for 16 days. At 10 p.m. on February 19, 1959, she took a total of 1,500 mg. of the drug, with suicidal intent, and retired to bed. For the first three-quarters of an hour she experienced no symptoms, and after this she apparently went to sleep. She has no recollection of any dreaming, and woke at 6.30 a.m. the next day in an agitated state, with gross involuntary movements of all her limbs, head, and neck, which she described as being just like those of a fit and of a violent and terrifying nature. She remained in this state for some time, being unable to shout for help. Eventually her mother brought her a morning cup of tea, and, seeing the gross movements, asked what was wrong. The patient was unable to tell her what had occurred, and was only able to mutter meaningless noises. She was, however, able to gesture towards the empty bottle of tablets.

During this period of involuntary movements she was quite conscious and clearly recollected what was happening, even though the movements were completely uncontrollable. She knew what she wanted to say, but was unable to articulate the words. After about one hour the movements in the limbs gradually diminished, those in the right leg being the last to subside. She had no headache, no difficulties with her vision, and no pain. There were paraesthesiae ("pins and needles") of the whole of her body, arms, and legs, and these continued for about one hour after the gross involuntary movements had ceased.

She was taken to the Bristol Royal Infirmary, where her stomach was washed out and the blood-pressure recorded as 100/70. Her admission to Barrow Hospital was then arranged.

On admission, at 10 a.m. on February 20, the most prominent feature was that of a state of over-alertness. Her face showed marked pallor, and the general appearance was that of anxiety. She was restless; she glanced rapidly around the room, and had a fine, rapid tremor of the hands. Her speech was jerky, rapid, and slurred. She had tachycardia (130 beats a minute) and the blood-pressure had risen to 130/90. Her temperature was 99.6° F. (37.55° C.). There was slight difficulty at first on passing urine, which was found to contain ketone bodies (Rothera's test). Her mouth was dry; she had a considerable thirst and no appetite. There was some increase of muscular tone of the cogwheel variety, tendon reflexes were normal, plantar responses were flexor, and objective sensory tests were normal. Her pupils reacted normally to light, but initially there was slight difficulty in accommodation. Her mental state did not appear to be impaired, and she could remember quite clearly the events of the past few hours. She could repeat eight digits forward and six backwards correctly. Her mood was one of depression and marked misery, but without any remorse or guilt because of her suicidal attempt.

Investigations.—Electroencephalograms taken on admission showed a record which was outside the normal limits and had a marked excess of slow activity (this could have been due to either imipramine-induced drowsiness or previous treatment with E.C.T.). Electrocardiograms showed simple tachycardia (rate 120); T wave flattened in lead II and inverted in lead III. Blood count was normal, with eosinophils 110/c.mm.

Progress.—During the next three days there was a gradual improvement in her condition without any special treatment being given. Mentally she remained depressed, and in view of this she was eventually given further E.C.T. The blood-pressure remained stationary, the fever settled, and the tachycardia disappeared.

COMMENT

The interesting features of this case are (1) the gross involuntary movements and dysarthria which occurred a few hours after taking the drug; (2) the lack of marked change of blood-pressure even though the drug has a methonium type of side chain; (3) the paraesthesiae and general atropine-like effects of the drug.

Three salient points are the inability of the drug to prevent a suicidal attempt while being used therapeutically (the dosage of 25 mg. t.d.s. is, however, smaller than the optimum recommended by the makers); the lack of improvement of depression following gross overdose; and the relative safety of the drug in this case when it was taken with suicidal intent.

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Reviews

SURGICAL PROGRESS

Operative Surgery. Under the general editorship of Charles Rob, *M.C.*, M.Chir., F.R.C.S., and Rodney Smith, M.S., F.R.C.S *Progress Volume, 1958. General Index.* (Pp. 100 +vii+9+76; illustrated. 60s.) London: Butterworth and Co. 1958.

What are the chief advancing points of operative surgery? Some indication may be found by looking through this progress volume for 1958 and noting the various operations described. As might have been anticipated, new techniques for operations on the heart and arteries, the liver and pancreas are well to the fore, while there is an operation for congenital atresia of the duodenum and another for stricture of the lower oesophagus associated with duodenal ulceration. Several of the procedures described appear formidable, but with modern advantages the removal of half the liver or the excision of the whole of the stomach and the lower oesophagus can be carried out safely. Nevertheless, one's confidence would be increased if there were added a table of results to indicate the average chance of success. Certainly the scope of surgery has considerably widened during the last few years, and progress is still being made. This volume contains an excellent general index and a useful index of contributors.

ZACHARY COPE.

THE OESOPHAGUS

Diseases of the Esophagus. By J. Terracol and Richard H. Sweet. (Pp. 682+xiii; illustrated. £7.) Philadelphia and London: W. B. Saunders Company. 1958.

Terracol, in his preface, says that the idea of writing a comprehensive book about the oesophagus originated before 1940 in the mind of Professor Belinoff, of Sofia. He unfortunately died, and Terracol took over the task. The first edition of his book achieved success because it correlated and explained an accumulation of isolated facts, opinions, and speculations. In 1952 Richard Sweet also decided to write a book about the oesophagus; but, says he, "I discovered that the task had already been accomplished in the French language by Professor Terracol and his collaborators . . . it seemed that an American edition, revised and modernized to include some of the newer knowledge, particularly regarding surgical treatment, would be of inestimable value." The present volume is the work of Terracol translated into English by Sweet, and to this Sweet has added his own experiences, opinions, and his results of surgical treatment.

It would not be an overstatement to say that Terracol and Sweet are universally regarded as masters of this topic, and no surgeon interested in the oesophagus can afford to be without this book. It is beautifully bound and printed. The text is clear and the illustrations and diagrams are excellent. There are 600 pages of text, and this is followed by a bibliography of 70 pages of references (chiefly French) in appropriate sections. The bibliography covers papers written during the last ten years—earlier papers are listed in Terracol's first edition.

The book covers the anatomy and physiology, congenital malformations, inflammations and growths, myoneural incoordinations and traumatic lesions, retained foreign bodies, psychological abnormalities, and all methods of investigation and treatment. Hiatus hernia is not mentioned. In most places the text is excellent. It is clear and helpful, and there are not many points to criticize. Terracol says that his object has been to eliminate repetition, confusion, and contradiction.

This book carries the hallmarks of French and American surgery. It contains but scant reference to the contributions and opinions of British surgeons, and it leaves one with the thought that the oesophagus is still the least understood part of the alimentary canal.

N. R. BARRETT.

MEAL-TIME MISERY

A Search for Man's Sanity. The Selected Letters of Trigant Burrow, with Biographical Notes. Prepared by the Editorial Committee of the Lifwynn Foundation: William E. Galt, Chairman. Foreword by Sir Herbert Read. (Pp. 615+xxi. 60s.) New York and London: Oxford University Press. 1958.

In his review of the book which Trigant Burrow regarded as his masterpiece—*The Neurosis of Man*—Dr. J. A. Hadfield quoted with approval the statement, "I experience a positive feeling of opposition every time I read Burrow's work" (*Brit. med. J.*, 1949, **2**, 1215). This man who aroused the hostility of the orthodox psychologists—Freud, Jung, and Adolf Meyer—found understanding, however, among his colleagues and disciples, and admiration among artists like D. H. Lawrence and Sir Herbert Read (who contributes a foreword to this book).

In 1923 Burrow gave up a large psycho-analytical practice in Baltimore in order to devote himself to the study of human behaviour. "Disorders in behaviour were for him essentially social or inter-relational, and demanded observation and study in their dynamic group setting." The group formed to analyse social behaviour consisted of 20 persons living in a camp in the Adirondacks. It can be imagined that conflicts were soon aroused, but, since human discord was their laboratory material, this situation had not only to be endured but to be encouraged. Human affections and family life were thrown into this unhappy melting-pot. "We did not flee," said Mr. Clarence Shields, Burrow's chief associate; "we stood by." Emotional situations were handled as material for objective analysis by the whole group, meeting three times a day round the dining-table. Whether anything emerged which justified this heroic dedication to a scientific objective must be left to the opinion of psychologists who have studied *The Biology of Human Conflict* and *The Neurosis of Man*. From these letters it is not apparent that Burrow's conclusions had any profound meaning for mankind. Perhaps, after all, Burrow and Shields did "flee," whether from the futility or from the pain of their self-immolation, for in their last period (1932–50) they became occupied with the internal physiological changes accompanying external behaviour—eye movements, brain-wave patterns, and changes in respiration.

Burrow's work has been criticized for the obscurity of its language and concepts, but there is nothing difficult in these letters, which are distinguished by the clarity of the writing, by their eloquence and humanity. Many of them were written to men and women who were his compeers in intelligence and distinction. The book is beautifully produced and elegantly printed. The abiding picture, however, is of meal-time misery in the Adirondacks. "That, my dear Clarence, you will agree is a clear example of projection which the group will discuss at dinner." No wonder that digestions became impaired and health undermined.

D. V. HUBBLE.

CLINICAL NEUROLOGY

The Neurologic Examination. Incorporating the Fundamentals of Neuroanatomy and Neurophysiology. By Russell N. DeJong, M.D. Second edition. (Pp. 1,078+xv; illustrated.) London: Pitman Medical Publishing Co., Ltd. 1958.

This is a fine publication and a useful work of reference. The author has almost a collector's enthusiasm for clinical tests, and he illustrates them well. Thus the methods of testing the strength of individual muscles are separately portrayed, as was done in the Medical Research Council's Wartime Memorandum, while an illustration of Strümpell's sign will revive memories among senior neurologists. The title is misleading, for no one could write 1,000 pages on methods of examination. This is in fact a book on anatomy, physiology, clinical methods, and diagnosis—an arrangement which reminds one of *The Diagnosis of Nervous Diseases*, by Purves-Stewart, which was so popular 25 years ago. This approach through anatomy and function is perhaps the best way to teach clinical neurology, so the student need not be frightened by the formidable size of this book.

W. RITCHIE RUSSELL.

OCCUPATIONAL ALLERGY

Occupational Allergy. Lectures Held During a Course on Occupational Allergy at The Hague in May, 1958. (Pp. 329+xvi; illustrated. Fl. 30.) Leyden: H. E. Steinfert Kroese N.V. 1958.

These lectures, all in English, deal with the general problems of allergy in industry and more specifically with the various occupational allergies. Many are review articles by European authorities, and some give accounts of original work. Most authors include a list of references.

Among chapters concerned with the general approach, Gerritsen's discusses the problems of pre-employment selection, the assessment of the sensitizing capacity of industrial materials, and protective measures of a personal and general kind. Williams analyses the social consequences of allergic disease, and Albahay deals with problems associated with compensation.

As one might expect, a large part of the book concerns the reactions of the skin, but nasal allergy, asthma, and allergic affections of the eye are also considered. There are chapters on the hazards of certain industries, among them the wool-textile trade, cigar manufacturing, baking, and printing. Malton contributes an erudite and thorough analysis of the skin-sensitizing effect of the numerous chemical agents employed by cotton-printers.

Although the subject is not exhaustively covered, the range of the lectures is sufficiently wide to form a useful reference book which can be recommended not only to those interested primarily in allergy but also to industrial physicians.

R. S. BRUCE PEARSON.

THE COLLECTIVE UNCONSCIOUS

The Objective Psyche. By Michael Fordham, M.D., M.R.C.P., F.B.Ps.S. (Pp. 214+vii. 25s.) London: Routledge and Kegan Paul. 1958.

In this collection of lectures on Jungian psychology, previously published separately and now reprinted, the author expounds some aspects of Jung's work, and in particular the hypothesis of the collective unconscious—that the psyche contains impersonal, objective, and autonomous elements. Jung himself considers his investigations on this theme as his most significant contribution. Yet none of his empirical concepts has met with so much misunderstanding. Some scientists think of Jung as a philosophical mystic, and possibly know little or nothing of his writings and feel no obligation to read them. This may be naive, but not necessarily prejudiced. If such critics chance to read the chapter on the objective psyche, which gives its title to this book, they will find it new and stimulating. Nevertheless, they may stumble when informed that archetypal images are "psychologically objective and can evidently be considered as the correlate of matter in other natural sciences." Most of the lectures were given to societies concerned with psychology and psychopathology, and readers unfamiliar with Jung's terminology will find them hard going.

There are three new essays on some psychological aspects of religion. The conclusion that religious experience is a projection and lacks objectivity will hardly appeal to the theologians. They will refute this supposition—not for the first time—and argue, in their turn, that religious experience derives from objective sources. Fordham modestly admits that the psychologist's estimate of religion may well be elementary and amateurish.

Jung, of course, makes no claim that his theory of the collective unconscious is scientifically and objectively true. He puts it forward as explaining the facts better than any other hypothesis. And this, it may be guessed, is Fordham's position despite his lapses into polemics.

E. A. BENNET.

X-RAY EXPOSURE AND PROCESSING

Principles of Radiographic Exposure and Processing. By Arthur W. Fuchs. (Pp. 284+xvi; illustrated. 80s.) Oxford: Blackwell Scientific Publications. 1958.

This book of 26 chapters emphasizes the practical aspects of exposure and processing, and numerous tests are outlined and illustrated. For some of the tests a live subject has been used; students should be warned that this is inadvisable. The illustrations of the test series are too small—some are no bigger than postage stamps. The larger half-tone reproductions are first-class. In Fig. 18 either the captions or the radiographs are in the wrong place, which will confuse the beginner.

Since students are tempted to skip chapters which appear mathematical, the author's attempt to explain phenomena without the aid of mathematical equations is commendable, although in the later chapters chemical equations do appear. But it is a pity he omits characteristic curves—one or two dealing with sensitivity and contrast of films, developers, and intensifying screens would be welcome, especially as in Great Britain students are expected to have a fundamental knowledge of such curves.

There are an excellent glossary of terms and an extensive bibliography. The glossary provides satisfactory and concise answers to viva-voce questions, though for written questions a student would need to look up some of the bibliographic references. Readers should be warned that the terminology and abbreviations are American, that the frequency of alternating-current supply is 50 per second in Great Britain, and that liquid measure in America is different—and translate accordingly. The book is splendidly produced. It is to be recommended as an introduction for a beginner, or as a useful addition to a student's library.

W. WATSON.

FRACTURES AND DISLOCATIONS

Die Knochenbrüche und Verrenkungen und ihre Behandlung. Ein Lehrbuch fur Studierende und Arzte. By Professor Egbert Schwarz. (Pp. 370+xv; illustrated. DM. 33.20.) Jena: Gustav Fischer Verlag. 1958.

The small textbook on fractures has assumed a standard form: there is usually a general section dealing with principles and their application, and appliances; followed by a specialized section on how to treat individual fractures and dislocations, starting with the skull and ending with the toes. Here is a convenient medium-sized volume along these lines setting out the standard treatment practised in Germany, and, as would be expected from the practical hands of the author, it differs very little from its English counterpart.

A few points call for comment. One would like to see traction on the thumb abandoned as the recommended treatment for Bennett's stave fracture. Greater emphasis could be laid on the nail and plate for pertrochanteric fractures in the elderly, and this device, rather than a Küntscher nail, might well be suggested for subtrochanteric fractures. Strapping half the chest for fractured ribs could well be abandoned because of its inefficiency, and complete circular strapping with an adhesive elastic bandage, which gives much greater support, substituted.

All the primary types of fracture are illustrated, though a few figures have crept in upside down. No undue emphasis is laid on open operative treatment, and the volume is an excellent and balanced guide for students and practitioners.

J. G. BONNIN.

CYCLOPROPANE ANAESTHESIA

Cyclopropane Anesthesia. By Benjamin Howard Robbins, B.A., M.S., M.D. Second edition. (Pp. 293+xii; illustrated. 72s.) London: Baillière, Tindall and Cox. 1958.

In the 20 years since the first edition of this book cyclopropane has been accepted as a valuable inhalational anaesthetic. Were it not inflammable it might be one of the most valuable. There is a real place, therefore, for a monograph as comprehensive as this one. The chemical and physical properties of the substance are reviewed, and both its effect upon the main organs and tissues of the body and the clinical uses are fully described; hardly a statement is made without support from published experimental evidence. The text is illustrated with numerous charts and tables. The references, 353 of them, are gathered at the end. This is an invaluable guide for research workers, pharmacologists, and anaesthetists.

W. W. MUSHIN.

The possible relationship between a high-fat diet and coronary and hepatic disease has led Alice Record Hooper to publish *Fat-free Cookery* (Oxford University Press, 1959; 112 pp., 12s. 6d.), a collection of fat-free recipes for all occasions. A list of foods permitted and foods forbidden is included.

The annual volume of the *National Library of Medicine Catalog* for 1958 has been published by the Card Division, Library of Congress, Washington, 25, D.C. (1,031 pp.; $17.50). This author and subject catalogue, which covers additions to the library during the period November, 1957, to October, 1958, as well as some recatalogued material, succeeds the library's bibliographical record begun in 1880 with the *Surgeon-General's Catalogue*, continued with the quinquennial (1950–4) and subsequent annual editions, and supplemented by the *Current List of Medical Literature*.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

The Child with Abdominal Pains. By John Apley, M.D., F.R.C.P. (Pp. 86+vii. 12s. 6d.) Oxford: Blackwell Scientific Publications. 1959.

Quantitative Studies on the Islets of Langerhans. By Bo Hellman. (Pp. 461–482.) Uppsala: Almquist and Wiksells Boktryckeri AB. 1959.

Miscellaneous Notes. (Fourth Series.) By F. Parkes Weber, M.D., F.R.C.P., F.S.A. (Pp. 32. 6s.) London: H. K. Lewis and Co. Ltd. 1959.

Biology Staining Schedules for First Year Students. By R. R. Fowell, M.Sc. Sixth edition. (Pp. 31; illustrated. 3s.) London: H. K. Lewis and Co. Ltd. 1959.

International Pharmacopoeia. First Edition. Supplement. Recommended Specifications. (Pp. 224+xx. 25s.) Geneva: World Health Organization. London: H.M. Stationery Office. 1959.

Cholera. By R. Pollitzer, M.D. With two chapters written in collaboration with W. Burrows, M.D., and S. Swaroop, Ph.D., M.P.H. (Pp. 1,019; illustrated. £5.) Geneva: World Health Organization. London: H.M. Stationery Office. 1959.

What is Unlawful? Does Innocence Begin where Crime Ends? Afterthoughts on the Wolfenden Report. By Quentin Edwards. (Pp. 14. 1s. 6d.) London: Church Information Office for Church of England Moral Welfare Council. 1959.

Histonomy of the Cerebral Cortex. By S. T. Bok. (Pp. 434+ix; illustrated. 72s.) Amsterdam, London, New York, Princeton: Elsevier Publishing Co. 1959.

The Fluids of Parenteral Body Cavities. By Paul D. Hoeprich, M.D., and John R. Ward, M.D. (Pp. 98+vi; illustrated. $4.75.) New York and London: Grune and Stratton. 1959.

The Campden Wonder. Edited by Sir George Clark. With Chapters by the late Viscount Maugham and Dr. D. Russell Davis. (Pp. 155; illustrated. 18s.) London, New York, Toronto: Oxford University Press. 1959.

A History of Biology to About the Year 1900. A General Introduction to the Study of Living Things. By Charles Singer. Third (revised) edition. (Pp. 580+xxxvi; illustrated. 50s.) London and New York: Abelard-Schuman. 1959.

The Process of Aging in the Nervous System. By 32 contributors. Edited by James E. Birren, Ph.D., Henry A. Imus, Ph.D., and William F. Windle, Ph.D., Sc.D. (Pp. 224+xii; illustrated. 52s. 6d.) Oxford: Blackwell Scientific Publications. 1959.

Coronary Heart Disease. By John William Gofman, M.D., Ph.D. (Pp. 353+xx. 60s.) Oxford: Blackwell Scientific Publications. 1959.

Radiation Biology of Vicia Faba in Relation to the General Problem. By John Read, B.Sc., Ph.D. (Pp. 270+xx; illustrated. 45s.) Oxford: Blackwell Scientific Publications. 1959.

Genetics, Radiobiology and Radiology Proceedings, Mid-Western Conference. By Wendell G. Scott, M.D., Chairman, and Titus Evans, Ph.D., Co-Chairman. (Pp. 149+xv; illustrated. 42s.) Oxford: Blackwell Scientific Publications. 1959.

Medical Radiographic Technic. Prepared by Technical Service, *X*-ray Department, General Electric Company, under the supervision of the late Glenn W. Files. Revised by William L. Bloom, Jr., John L. Hollenbach, R.T., James A. Morgan, R.T., and John B. Thomas, R.T. Second edition. (Pp. 386; illustrated. 82s. 6d.) Oxford: Blackwell Scientific Publications. 1959.

The Megaloblastic Anemias. By Victor Herbert, M.D. (Pp. 162+vi; illustrated $6.) New York and London: Grune and Stratton. 1959.

British Chemicals and their Manufacturers. The Directory of the Association of British Chemical Manufacturers (Incorporated). (Pp. 207.) London: Association of British Chemical Manufacturers. 1959.

Leitfaden der Mikroskopischen Technik. Mikroskopische, Präparative und Färberische Verfahren in der Histologie. By Dr. Herbert Haug. (Pp. 218+xii; illustrated. DM. 29.80.) Stuttgart: Georg Thieme Verlag. 1959.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY DECEMBER 26 1959

HYPERTENSION AND THE KIDNEY

When Richard Bright drew attention to the relation between renal disease and enlargement of the left ventricle he could hardly have foreseen the great volume of study and research which would come to link renal disease with hypertension. The association of hypertension with acute and chronic nephritis has been long recognized, and more recently the importance of chronic pyelonephritis as a cause of hypertension has been stressed.[1] Other renal diseases which may cause hypertension are polyarteritis nodosa, polycystic disease, intercapillary glomerulosclerosis (Kimmelstiel–Wilson kidney), radiation nephritis, stenosis of the renal artery, systemic lupus, scleroderma, tuberculosis, nephrocalcinosis, and toxaemia of pregnancy.

In his Goulstonian Lectures, reproduced in this and last week's *Journal*, Professor W. S. Peart has reviewed the association between high blood-pressure and renal disease, pointing out that not all types of renal disease lead to hypertension, which tends to be confined to those causing extensive glomerular damage, for severe renal failure without hypertension may result from tubular necrosis alone. But in cortical necrosis, where glomeruli are involved, hypertension is common. It is not known whether reduction in blood supply to the glomeruli removes an antihypertensive action possessed by normal glomeruli or whether a pressor substance is formed in ischaemic glomeruli. Changes in glomerular function may lead to hypertension before any evidence of structural change has appeared, as has been shown in experimental radiation nephritis.[2]

The relationship of pyelonephritis with hypertension has in the past been questioned, but good evidence in support of this concept is now available. Pyelonephritis is often unilateral, and P. Kincaid-Smith[3] has suggested that partial or complete arterial obstruction is the basis of hypertension in this disorder. There is now abundant evidence that reduction of blood supply to the glomeruli can result in hypertension. Professor Peart points out that hypertension can exist in the absence of organic occlusive disease in the renal arteries, when perhaps vasoconstriction may lead to reduction of blood supply. Organic arteriolar changes tend to be associated only with long-standing hypertension. Evidence of the connexion between arterial occlusion and hypertension is best provided by stenosis of the renal artery, now being more often recognized as an important cause of serious hypertension.

Professor Peart, in his second lecture, discusses the possible ways in which the kidney may cause hypertension. These are: failure to excrete or destroy an extra-renal pressor substance; failure to produce a vasodilator; increased responsiveness of normal pressor mechanisms; decreased response of baroreceptors; stimulation of an extrarenal pressor system (such as the adrenal gland); redistribution of water and electrolytes; and production of a vasoconstrictor substance. Failure to excrete alone cannot be a cause, for hypertension persists in the nephrectomized dog even when the blood urea is kept down by dialysis. Extrarenal factors are brought into play, however, as shown by G. W. Pickering,[4] who showed that in the rabbit with unilateral occlusion of the renal artery (the other kidney having been removed) excision of the ischaemic kidney within eight days was followed by a fall in blood-pressure. But if the kidney was removed after eight weeks the hypertension persisted. Partial occlusion of one renal artery in rats causes sustained hypertension, which may persist after removal of the clamped kidney as a result of vascular lesions in the unclamped kidney caused by the hypertension.[5] In man, however, a fall in blood-pressure can occur after unilateral nephrectomy even when hypertension has been established for many years.[6]

Evidence for the importance of failure of production of a vasodilator substance, or for increased responsiveness of normal pressor mechanisms (such as sympathetic hypertonia or enhanced sensitivity to noradrenaline) is, in Professor Peart's view, scanty, as is that for increased responsiveness of baroreceptors. The suggestion that renal disease might stimulate the adrenal gland to increase the blood-pressure received support from H. Goldblatt's[7] observation that in the dog adrenalectomy would prevent hypertension due to constriction of the renal artery. Although there is

[1] Kincaid-Smith, P., McMichael, J., and Murphy, E. A., *Quart. J. Med.*, 1958, **27**, 117.
[2] Wilson, C., Ledingham, J. M., and Cohen, M., *Lancet*, 1958, **1**, 9.
[3] Kincaid-Smith, P. ibid., 1955, **2**, 1263.
[4] Pickering, G. W., *Clin. Sci.*, 1945, **5**, 229.
[5] Wilson, C., and Byrom, F. B., *Quart. J. Med.*, 1941, **10**, 65.
[6] Pickering, G. W., and Heptinstall, R. H., ibid., 1953, **22**, 1.
[7] Goldblatt, H., *Ann. intern. Med.*, 1937, **11**, 69.
[8] Pickering, G. W., *High Blood Pressure*, 1955. London.
[9] Arnott, W. M., Crooke, A. C., Donovan, H., and Taylor, S. H., *Quart. J. Med.*, 1957, **26**, 501.
[10] Conn, J. W., *J. Lab. clin. Med.*, 1955, **45**, 6.
[11] Milne, M. D., Muehrcke, R. C., and Aird, I., *Quart. J. Med.*, 1957, **26**, 117.
[12] Dollery, C. T., Shackman, R., and Shillingford, J., *Brit. med. J.*, 1959, **2**, 1367.
[13] Platt, R., *Quart. J. Med.*, 1948, **17**, 83.
[14] Hodson, C. J., *Proc. roy. Soc. Med.*, 1957, **50**, 539.
[15] Poutasse, E. F., and Dustan, H. P., *J. Amer. med. Ass.*, 1957, **165**, 1521.
[16] Yates-Bell, J. G., *Brit. med. J.*, 1959, **2**, 1371.
[17] Harington, M., Kincaid-Smith, P., and McMichael, J., ibid., 1959, **2**, 969.

evidence that the adrenal gland may be concerned in the aetiology of essential hypertension,[8] and although adrenalectomy has achieved some success in the treatment of severe essential hypertension in man[9] and excessive production of aldosterone by the adrenal cortex may be associated with hypertension,[10 11] the importance of this gland in renal hypertension is uncertain.

As to water and electrolytes, there is no constant relation between the total amount of sodium in the body and the level of the blood-pressure, although excessive intake of sodium is accompanied by a rise in blood pressure and vice versa. While there is undoubtedly an abnormality in the handling of sodium and water by the kidney in hypertension, this is a secondary rather than a primary occurrence, as Peart shows. Hypertension may be associated with loss of potassium via the kidney,[10 11] but this in some cases is probably the result of pre-existing renal disease which has caused the hypertension.[12]

The production of vasoconstrictor substances in the ischaemic kidney has been extensively investigated. Renin, an enzyme produced by the ischaemic kidney, acts upon a substrate in the plasma to produce hypertensin (angiotonin). Both these substances are active in raising the blood-pressure, but, surprisingly, Peart was not able to obtain renin from renal-vein blood in rabbits made hypertensive by clamping the renal artery, as might be expected. A study of the action of hypertensin in man might clarify its importance in hypertension. In normal subjects hypertensin reduces blood flow in the hand, as do adrenaline and noradrenaline. But blood flow in the hand is normal in unilateral renal disease with hypertension, in contrast to phaeochromocytoma (in which adrenaline and noradrenaline are circulating). The circulatory effects of hypertensin are vasoconstrictive and do not, apparently, harmonize with any of the findings in renal hypertension except perhaps those in acute nephritis.

Peart concludes that investigations in man and experiments in rabbits indicate that renin cannot be wholly, if at all, responsible for renal hypertension. Clearly further work remains to be done, and, although much has been elucidated, each new discovery brings further problems in the mechanism of renal hypertension.

From the clinical aspect, however, valuable knowledge has been gained about the part played by the kidney in hypertension. It is generally accepted that serious hypertension under the age of 40, and certainly under the age of 30, is most unlikely to be "essential" in type, and that if adrenal tumour and coarctation of the aorta are excluded a renal cause is probable.[13] While many patients will have bilateral renal disease, a vigorous search for a removable unilateral renal lesion must be made. The importance of stenosis of the renal artery and of pyelonephritis (which may be unilateral) has already been mentioned. Obstruction of the renal artery may be diagnosed by renal arteriography, performed by retrograde aortic injection through the femoral artery,[14] and this investigation should always be considered in subjects with worsening and serious hypertension, especially if the kidneys are of normal or unequal size or shape.[15 16] Elderly patients are often affected by obstruction of the renal artery, but premature atherosclerosis can occur in young people. P. Kincaid-Smith and her co-workers[1] noted that hypertensive vascular changes were absent from the ischaemic kidney in four patients with malignant hypertension and obstruction of the renal artery, suggesting that the obstruction preceded the hypertension, which resulted from a "Goldblatt effect." The place of renal biopsy in the investigation of hypertension is not yet fully decided,[16] but it may be very helpful in clearing up the aetiology in difficult cases (such as polyarteritis nodosa) and in detecting changes in the supposedly healthy kidney of patients with a predominantly unilateral lesion. Divided renal function tests are also of value in assessing individual renal function.[12 16]

Hypertension due to unilateral renal disease may on occasions be dramatically cured by nephrectomy.[8] In last week's *Journal* J. G. Yates-Bell[16] reported that in 66 patients who had a nephrectomy for hypertension the cure rate was 46%, the criterion for cure being a diastolic pressure of 90 mm. Hg for one year after operation. The results were better in younger subjects, those over 50 years of age seldom benefiting unless the hypertension was recent. Nephrectomy is usually contraindicated if total renal function is impaired.[8]

Reconstruction of obstructed renal arteries offers a hopeful approach to the treatment of hypertension, but nephrectomy is often preferable when the other kidney is healthy, owing to risk of recurrence of the vascular lesion or of permanent damage to the diseased kidney.[16] C. T. Dollery and his colleagues[13] report two patients with obstruction of a renal artery and malignant hypertension treated by nephrectomy: in one the hypertension was cured, but in both patients hypokalaemia due to loss of potassium from the kidneys was relieved, suggesting that the loss was due to ischaemic tubular damage.

These recent experiences show that relief of serious hypertension can be achieved by surgery in selected cases with unilateral renal disease. Thorough investigation of the young hypertensive patient is thus a matter of great importance. The majority of such

patients will be found to have bilateral disease, and for them the effective hypotensive drugs offer the best hope of improvement. It is reassuring to know that in malignant hypertension the expectation of life may thus be increased by a factor of six to eight times that expected without treatment,[17] although severe renal or cerebral vascular disease often results in death from uraemia or cerebral vascular accident irrespective of the control of the blood-pressure. The prognosis in this group could doubtless be improved further if the diagnosis were made earlier and effective treatment begun before irreversible renal and other vascular damage has occurred.

AMPHETAMINE IN ATHLETICS

Two years ago the American Medical Association decided to investigate the charge that there was a widespread use of amphetamine to improve athletic performance. Three national athletic associations co-operated, and the committee which was appointed consulted physicians and others connected with sport; they reached the conclusion that the use of amphetamine and related substances was very small. One member of the committee, however, Dr. H. K. Beecher, who is professor of anaesthetics, undertook an investigation in Harvard to see whether in fact amphetamine did improve athletic performance, and the results of this investigation have recently been published.[1]

The work was done with great care and the results bear every mark of reliability. The subjects were students at college, and the forms of effort investigated were swimming, running, and putting the weight. The scale of the trial is indicated by the first experiment, which provided 360 timed performances by 15 swimmers over 100 and 200 yards (90 and 180 metres). Each swimmer swam four times after having been given a dummy tablet, four times after having been given amphetamine, and four times after having been given secobarbital (quinalbarbitone). The dose of amphetamine was large, 14 mg. per 70 kg. body weight, which means approximately 14 mg. per man. The swimmer did not know what he was receiving, and the secobarbital was included in the trial so that when his feelings indicated that he was affected by a drug he should not jump to the conclusion that he was receiving amphetamine.

Amphetamine certainly increased the performance. Thus all save one swam more quickly when receiving amphetamine. The mean improvement was, however, only 1.26 seconds on a time which was about 65 seconds for 100 yards and 160 seconds for 200 yards. Statistically the difference was significant. As might be expected, the performance of 14 out of 15 subjects was impaired by secobarbital. The subjects were allowed 15 minutes' rest after the first swim, and then repeated the swim when they were still fatigued. The improvement due to amphetamine was less in the second swim. The amphetamine was given two to three hours before the swim because earlier observations had suggested that this was the interval required for maximum effect. In order to encourage everyone to do his best the subjects were told that each man whose mean time under experiment was equal to or less than his mean time when actually competing would be given a steak dinner where he could order anything he wanted up to 7.50 dollars.

Similar results were obtained in tests of running over distances from 600 yards (550 m.) to 1 mile (1.6 km.). The mean increase in performance after amphetamine was about 4 seconds on times from 90 to 300 seconds. As before, one subject did worse with amphetamine than without it. Those putting the weight (35 lb.—16 kg.) increased their distance by a mean value of 2.5 ft. (76 cm.) when taking amphetamine.

A similar investigation was also undertaken by P. V. Karpovich.[2] He found that out of 54 college students taking doses of 10 or 20 mg. one-half to one hour before the test, the performance of 50 was unaffected, the performance of 3 was improved, and the performance of one was made worse. In a leading article commenting on these findings, the *Journal of the American Medical Association* draws attention to the illegal traffic in the amphetamines in the U.S.A., and urges doctors not to prescribe these drugs for athletes.

[1] G. M. Smith and H. K. Beecher, *J. Amer. med. Ass.*, 1959, **170**, 542.
[2] P. V. Karpovich, ibid, 1959, 558.

CEPHALOSPORIN C

Antibiotics are evidently considered to be news. The daily press early last week led its readers to believe that a remarkable discovery has been made in cephalosporin C: even the expression "break-through" was used, suggesting final success in a prolonged and difficult effort. The basis of this announcement is an item in the report[1] of the National Research Development Corporation. This, after explaining briefly why this antibiotic is believed to have some promise of usefulness, only records that "much effort is being devoted to" determining its structure, and that the Corporation "has arranged to associate a large British antibiotic-

[1] National Research and Development Corporation, Report for the year 1958-59. H.M.S.O., London. Price 1s. 3d. net.
[2] Florey, H. W., *Ann. intern. Med.*, 1955, **43**, 480.
[3] See annotation, *Brit. med. J.*, 1959, **2**, 628.
[4] Henderson, N. D., and Olson, B. H., ibid., 1959, **2**, 1404.
[5] Crawford, K., and Abraham, E. P., 1957, *J. gen. Microbiol.*, 1957, **16**, 604.

producing firm to help in those aspects of the work requiring larger scale preparation facilities. . . ." This work has in fact been going on for five years, and the yield of cephalosporin C obtained by present fermentation methods has been so small as to have hampered even the earlier stages of its laboratory study. Unless a much larger yield can be secured commercial production must remain only a remote possibility.

The story of the discovery of this antibiotic is one of the strangest in a field of study which has produced many odd incidents. The organism forming it, a *Cephalosporium*, was cultivated from the sea near a sewage outfall on the coast of Sardinia by Brotzu, who found that cultures of it had antibiotic activity and used an extract with some success for treating enteric fever and brucellosis. These findings were published only in an obscure Sardinian journal, and it was not until three years later that a culture reached Oxford, where it was soon found that the organism produced not one antibiotic but several.[2] One of these is cephalosporin N, now known to be identical with synnematin B, which was obtained from a different species: this substance is a form of penicillin, with an activity directed mainly against Gram-negative organisms. It has since been used with success for the treatment of typhoid fever,[3] and other infections,[4] and is presumably the element in the crude extract used by Brotzu which achieved such therapeutic success as he observed. Cephalosporin P has a high activity against staphylococci, but for several reasons, including the rapid acquisition of bacterial resistance to it, has been deemed unlikely to prove useful therapeutically.

A third component, cephalosporin C, is the subject of the present public interest. This substance has some chemical relationship to penicillin, and has a similar antibacterial spectrum, but on a lower level of activity against staphylococci and streptococci. It is remarkably non-toxic and therapeutically active in mice when given by injection. Little is absorbed from the alimentary tract. Its property which has excited most interest is that it is resistant to staphylococcal penicillinase and competitively inhibits the action of this enzyme on penicillin. Thus mixtures of cephalosporin C and penicillin act synergically, at least *in vitro*, on penicillin-resistant staphylococci.[5] Fairly high concentrations of one or both are necessary to achieve this effect, and it has yet, so far as we are aware, to be shown to occur *in vivo*. Nevertheless any prospect of thus being able to deal with one of the most difficult of all infections is attractive, and there is always the possibility, as in the parallel studies which are now going on of penicillin itself, that further manipulation of the molecule may improve its performance.

THE BRITISH COUNCIL IN 1958–9

"It is the British Council's role to extend the area of contacts (overseas) beyond the normal diplomatic and commercial limits and to forge contacts in the educational, scientific, professional, and cultural worlds," says Sir Paul Sinker, the council's director-general, in the *Annual Report for 1958–9*. One of the council's main problems now is manpower—and first-rate manpower—for demands on it are increasing and it has entered a period of fairly rapid expansion. "In all our work," he observes, "we seek a practical advantage . . . we are neither do-gooders nor propagandists," and he sees service with the council as offering scope for practical idealism and the spirit of adventure.

In the past five years the council's gross annual income has almost doubled, from £3m. to £6m., and four-fifths of its resources are being spent in the developing areas of the world—the Near and Middle East, South and South-East Asia, and Africa. There is a great demand for scientific and technical teachers, which is only damped down by the shortage in this country, and an increasing number of visitors coming here for scientific and technical purposes. The numbers of overseas students here have grown from 10,000 in 1950 to 40,000 now. The centre of the British Council overseas is the library, and plans for making easier the circulation of British books are already under way. Among the council's own publications are the *Medical Book List* and the *British Medical Bulletin*, which has gone on from strength to strength as one of the outstanding contributions to current medical knowledge. Under its director, Dr. Margaret Suttill, the medical department of the British Council has done yeoman work in arranging courses in Britain for foreign graduates and sponsoring lectures by British doctors abroad. This side of the British Council's activities deserves the fullest support and encouragement.

A NEW ANGLE ON SMOKING

Circumstantial evidence that cigarette smoking is a direct and important cause of cancer of the lung continues to accumulate. The great majority of Seventh Day Adventists are non-smokers, and from a recently published study[1] it appears that they are much less likely to be admitted to hospital for lung cancer than the rest of the population in which they live. In eight hospitals under the direction of the Seventh-Day Adventist Church, the medical records of all patients diagnosed over a specified period as having cancer were scrutinized. Among the men admitted to hospital who were not Seventh-Day Adventists there were 158 cases of lung cancer. Among those who were members of this church, approximately 9.4% of all admissions, about 15 cases would have been expected. There were

[1] Wynder, E. L., Lemon, F. R., and Bross, I. J., *Cancer (Philad.)*, 1959, **12**, 1016.
[2] Edwards, J. H., *Brit. J. prev. soc. Med.*, 1957, **11**, 10.
[3] Haenszel, W., Shimkin, M. B., and Mantel, N., *J. nat. Cancer Inst.*, 1958, **21**, 825.
[4] Berkson, J., *Proc. Mayo Clin.*, 1955, **30**, 319.
[5] Fisher, R. A., *Smoking. The Cancer Controversy*, 1959, Edinburgh.
[6] Kennaway, E., *Brit. med. J.*, 1957, **1**, 299.
[7] Wynder, E. L., Bross, I. J., and Feldman, R. M., *Cancer (Philad.)*, 1957, **10**, 1300.
[8] Doll, R., and Hill, A. B., *Brit. med. J.*, 1956, **2**, 1071.
[9] Hammond, E. C., and Horn, D., *J. Amer. med. Ass.*, 1958, **166**, 1159.
[10] ——, —— ibid., 1958, **166**, 1294.

in fact only two. Significantly, there were also two cases among the Seventh-Day Adventist women, which is in keeping with the suggestion[2 3] that in the absence of smoking mortality from lung cancer would be the same in both sexes.

The importance of this observation lies less in the fact that it is in accord with the considerable body of evidence in support of the belief that tobacco smoke is, directly or indirectly, carcinogenic than that it makes less likely the hypothesis that the well-documented association between cigarette smoking and lung cancer is not a causal one.

It has been suggested that the association is determined by the individual genotype,[4 5] with the implication that certain people inherit a predisposition both to lung cancer and to smoke cigarettes. To accommodate such a hypothesis to these new data it would be necessary to stipulate also a genetic predisposition not to belong to the Seventh-Day Adventist Church.

The study was not confined to cancer of the lung. It was also found that the number of cases of cancer of the mouth, larynx, and oesophagus among members of the sect was only one-eighth of that expected. Since Seventh-Day Adventists are non-drinkers as well as non-smokers, this is in agreement with previous reports that there is an association between heavy drinking and cancer of these sites.[6 7] Among patients who were not Seventh-Day Adventists there were twice as many males as females with myocardial infarction. Among members of the church, however, the sex ratio was approximately 1:1, the number of males being considerably less than expected, particularly in the younger age group. This is also in line with previous reports that there is an association between cigarette smoking and disease of the coronary arteries.[8–10]

To many it will come as no surprise to learn that the benefits of religious observances are by no means restricted to the future life. But not often before can the evidence have been put on such a sure statistical basis.

CHRISTMAS FARE IN HOSPITAL

The sternest dietitians have probably always looked at Christmas pudding with some suspicion. According to a recent report[1] from St. Thomas's Hospital Christmas pudding was condemned as unsuitable for patients two hundred years ago. Many other kinds of food were also banned, including fish and tripe-and-onions. Even fruit was viewed with disfavour and patients were blamed for buying it. The hospital records go back over 400 years, and about 1550 the patients' diet consisted mainly of bread, beef, and beer. Up to the middle of the last century weak beer brewed in the hospital was the patients' ordinary drink: only the governors enjoyed tea and coffee. "There were constant complaints that patients and nurses brought in strong beer contrary to the regulations." Apparently the medical staff managed to avoid this criticism. The report also observes that until the beginning of the last war there seemed to be a tendency to supply only the bare necessities in the way of diet, and the patients had to depend to a certain extent on their visitors to supplement the hospital food. At Christmas-time the sister of the ward purchased provisions for ward parties and so on, and often had to supplement the funds available for this from her own meagre pay. The nationalization of hospitals should at least have put an end to the need for this.

The report from St. Thomas's fails to explain the reason for the condemnation of Christmas pudding, and Dr. P. H. Friedlander does not mention it as a suspected cause of dyspepsia in his interesting paper about food and indigestion (see p. 1454). Nevertheless, about the time this issue of the *Journal* is landing on British doormats there will be quite a few people having reason to suspect that a slab of Christmas pudding lavishly embellished with brandy-butter was not the ideal substance for topping-up an already overloaded stomach. Perhaps it is just as well that Christmas pudding has not been used as a test substance in investigations of dyspepsia. A patient who had had a radio-opaque tube passed through his nose into his stomach before being invited to enjoy half a pound of Christmas pudding might have been tempted to echo some of the remarks reputedly made by the inmates of a certain workhouse one Christmas day long ago.

[1] *St. Thomas's Hospital Report for 1958-59.*

NUTMEG POISONING

Probably it would greatly surprise the housewife of the present day if she were told, as she grates her nutmeg over the rice pudding, that some fifty years ago the poisonous properties of this substance were the subject of a serious discussion at the Royal Society of Medicine.[1] At the turn of the century it was popularly known to have many more uses than as a mere flavouring agent. It figured in the pharmacopoeia of the quack; one whole nutmeg in a glass of stout or in hot water before retiring was held in these circles to be invaluable for colds and constipation; it was used to induce abortion as well as the menses. The occasional surprising results formed the subject of a number of reports in this and other journals.

The active toxic factor in nutmeg is myristicin, which is contained in the volatile oil. Nutmeg in a dose of 5 g. or more (the usual nutmeg weighs about 5 g.) can produce serious effects. Ingestion of smaller quantities has been known to cause such immediate effects as

[1] Dale, H. H., *Proc. roy. Soc. Med.*, 1908, **2**, Sect. 69.
[2] Gibbins, K. M., *Brit. med. J.*, 1909, **1**, 1005.
[3] Dodge, W. T., *Med. Rec. (N.Y.)*, 1887, **32**, 624.
[4] Wallace, G. B., *Contrib. Med. Res. (Vaughan)*, Ann. Arbor Mich., 1903, 351.
[5] Green, R. C., Jr., *J. Amer. med. Ass.*, 1959, **171**, 1342.

flushing of the skin, general itching, oedema of the face and eyelids, and shock, all of which suggests that some people may be hypersensitive to the substance.[2] Apart from hypersensitivity reactions, the toxic effects produced include abdominal pain, with or without vomiting, narcosis sometimes varied by delirium, fear of impending death (emphasized in almost all reports), hypotension, dyspnoea, tachycardia, cyanosis, dilatation of pupils, and absent reflexes. The onset of these effects is in from one to seven hours. Usually complete recovery follows after 24 hours or more, but death has been reported.[3] It may be added that, in many cases in which the nutmeg was intended to dislodge the foetus, in spite of the development of the serious effects described its target was found at the end of it all to be still firmly in position.

Experimental work, carried out by G. B. Wallace[4] and by H. H. (now Sir Henry) Dale[1] on cats, showed that fatty degeneration of the liver was produced by large doses. The finding of albumin in the urine also suggested renal damage. Dale held that serious effects on the central nervous system of man are produced by doses too small to cause liver damage. Biochemical investigation of cases of nutmeg poisoning has been limited by their rarity since the beginning of the century, but the report of a recent case[5] in the U.S.A. serves to show that they may still occur. The subject was a woman of 28 who took 18.3 g. of nutmeg to induce the menses. The clinical course followed that of the earlier reports. Serial studies of hepatic function as well as liver biopsy revealed no evidence of hepatic damage. Studies of renal function suggested a transient toxic effect on the kidneys. Acidosis was noted, with lowered levels of sodium and potassium in the serum during the crisis.

HEALTH IN RHODESIA AND NYASALAND

A recently published report[1] gives much useful information about the state of the public health in the Federation of Rhodesia and Nyasaland. After five years of federation there are still differences between the medical services available to the populations of the three states. Each has an African population of similar size —Southern Rhodesia 2,550,000, Northern Rhodesia 2,200,000, and Nyasaland 2,690,000—but the respective numbers of registered medical practitioners are 619, 295, and 71. Nevertheless, annual recurrent expenditure on medical and health services since 1953 has trebled in Nyasaland and doubled in Northern Rhodesia, compared with the more modest advance of 70% in Southern Rhodesia. Medical treatment is free to Africans, and in Nyasaland, the worst-served territory, there are 1.3 hospital beds of all descriptions per 1,000 of the population. Nearly all African hospitals are overcrowded, and more beds will be provided when the recently instituted system of hospital records has provided adequate information on which to estimate the type of extra accommodation required in different areas. Missions of many denominations, with the aid of Government subsidies, run no fewer than 186 medical stations in the three territories.

The annual average increase in the African population is such that the population is expected to double itself within thirty years, and this rate may well increase as malaria and the diseases of insanitation are brought under control. Malaria is uncontrolled and hyperendemic in Northern Rhodesia and Nyasaland except in urban and mining areas. Southern Rhodesia, where the notorious vector *Anopheles gambiae* is near the southern extreme of its range and does not present as intractable a problem as elsewhere, is the first mainland territory of tropical Africa to plan the actual eradication of malaria. Here the urban islands where the disease has been mastered are to be extended and joined; the protected zone will eventually increase to include the whole country, and will be maintained by preventive measures in a barrier zone around the periphery. In Southern Rhodesia, too, the control of bilharziasis (hitherto a problem even more intractable than that of malaria carried by *A. gambiae*) by practical and reasonably economical measures is confidently expected. Trypanosomiasis, despite the disturbance of human and animal life resulting from the building of the Kariba dam, is now a rare disease.

While the specifically tropical diseases decline, those due to increasing contact with civilization, such as tuberculosis and overt poliomyelitis, are on the increase. In Southern Rhodesia, where case-finding among contacts, mass-miniature radiography, and Mantoux testing on a large scale are all under way, the notification rate of tuberculosis (all forms) in 1958 was 142.1 per 100,000 compared with 124.8 in 1957. In the other territories less efficient case-finding may largely account for the lower figures. Progress is being made in the provision of hospital beds for patients with tuberculosis and of out-patient facilities for the supervision of those with arrested disease, but the report indicates that further steps will have to be taken to reduce the menace of tuberculosis. There was no poliomyelitis epidemic in 1958, but according to the notifications the incidence in Africans and non-Africans was 1.9 and 9.3 respectively per 100,000 (the figure in England and Wales was about 4.4), and it is obvious that the African population is reacting to the poliomyelitis virus more and more according to the European pattern. Efforts to get the population vaccinated against poliomyelitis are being met with apathy at present.

In the population of European origin the birth rate was 28.4 per 1,000 and the infant mortality rate 22.0 per 1,000 live births. There were only two maternal deaths during the year. The Europeans are few in number compared with the Africans—287,300 in all three territories, of whom 207,000 live in Southern Rhodesia—but according to the vital statistics they present a striking picture of a vigorous and healthy community.

[1] *Annual Report on the Public Health of the Federation of Rhodesia and Nyasaland for the Year 1958.* Printed by the Government Printer, Salisbury, 1959. Price 10s. 6d.

Clinicopathological Conference

A CASE OF BRONCHIECTASIS WITH OSTEOPOROSIS

DEMONSTRATED AT THE

POSTGRADUATE MEDICAL SCHOOL OF LONDON

This is the case of a man with bronchiectasis whose death was accelerated by a rapidly progressive kyphosis (Case No. 161,617; P.M. No. 8,429).

Clinical History

Dr. C. M. FLETCHER: This man, an electric-truck driver, was aged 59 when he was first seen in the out-patient department of Hammersmith Hospital in April, 1954. He had always been healthy apart from gonorrhoea in the first world war and some form of dermatitis, three years previously, which had been treated with an arsenical medicine. He denied any cough (although he smoked 25 cigarettes daily), until January, 1954, when he developed a cough with profuse greenish-yellow sputum. He also became wheezy and slightly short of breath. He stopped smoking, but his symptoms continued until he first attended an out-patient clinic in April, 1954. The chest radiograph showed extensive chronic inflammatory changes (Fig. 1). A diagnosis of chronic bronchitis and emphysema was made. He was given a course of breathing exercises and discharged.

His symptoms persisted until January, 1955, when I first saw him. He was now more short of breath and had lost a stone (6.4 kg.) in weight. On examination he had a marked "snowflake" pigmentation of the skin and hyperkeratosis of the palms and soles, due to his arsenical medicine which he had recently discontinued. (This arsenical dermatitis subsequently cleared up.) He had slight kyphosis (Fig. 2) and widespread basal rales. The chest radiograph was

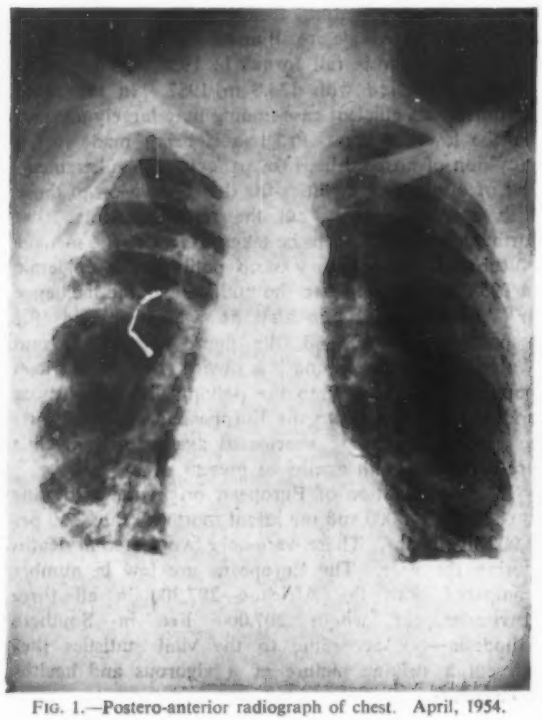

FIG. 1.—Postero-anterior radiograph of chest. April, 1954.

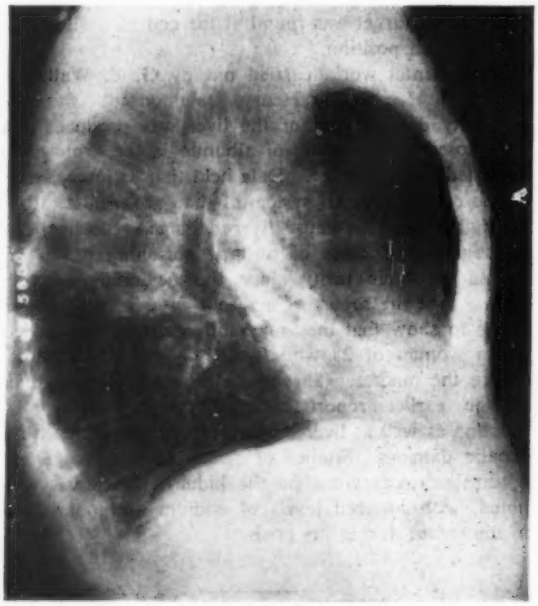

FIG. 2.—Lateral radiograph of chest. March, 1955.

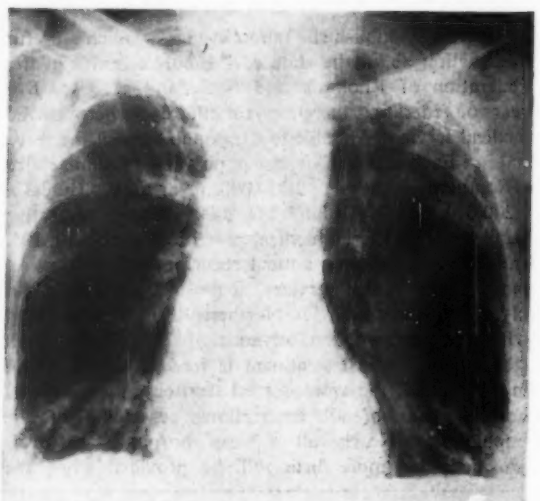

FIG. 3.—Postero-anterior radiograph of chest. January 1957. Note shadows at both apices and bases. Compared with Fig. 1 there is crowding of the upper ribs indicating increased kyphosis.

al radiograph of chest. August, 1957. Arrows indicate the collapsed vertebrae.

FIG. 5.—Radiograph of right hand. August, 1957. A normal metacarpal is shown for comparison.

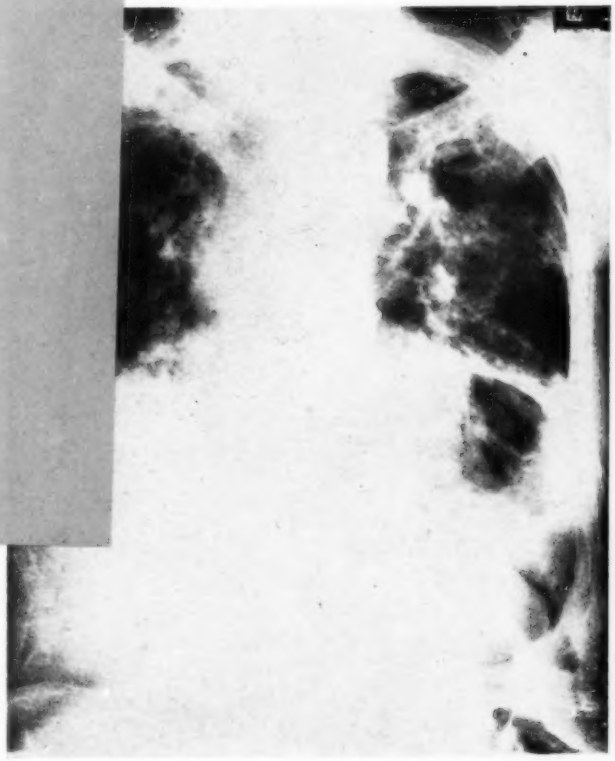

FIG. 6.– Postero-anterior radiograph of chest. May, 1958. Note overlap of ribs and iliac crest.

FIG. 7.—Lateral radiograph of chest. May, 1958. Note the ribs overlapping the iliac crest.

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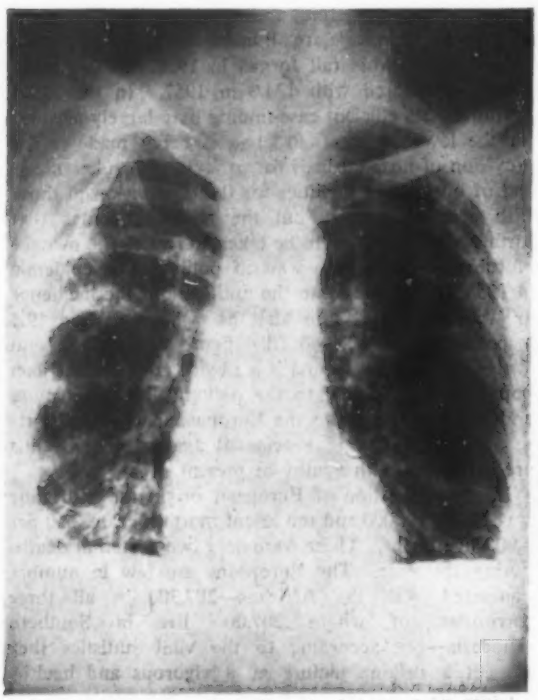

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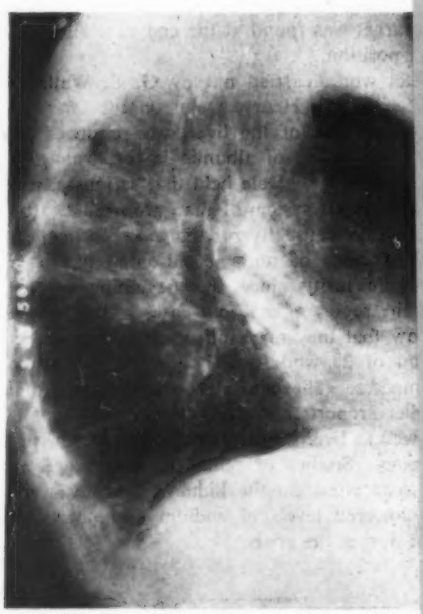
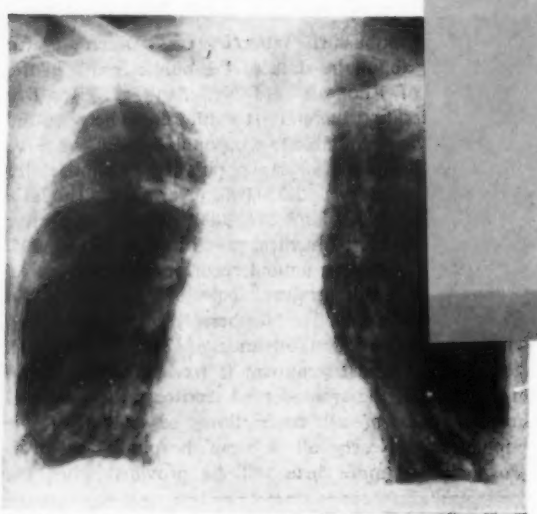


FIG. 2.—Lateral radiograph of chest. March



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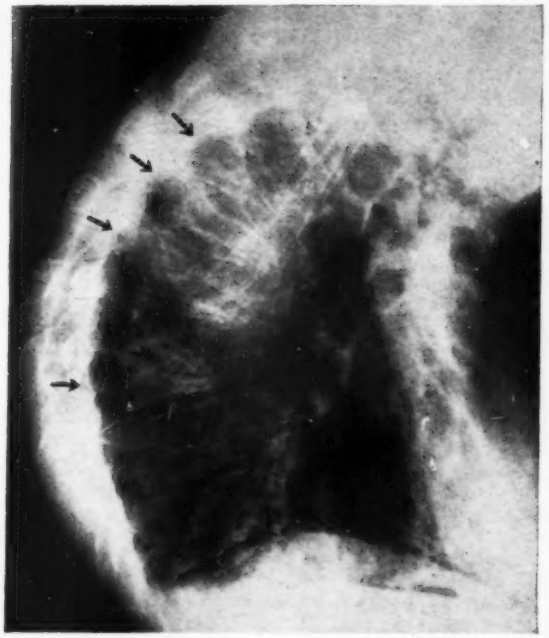
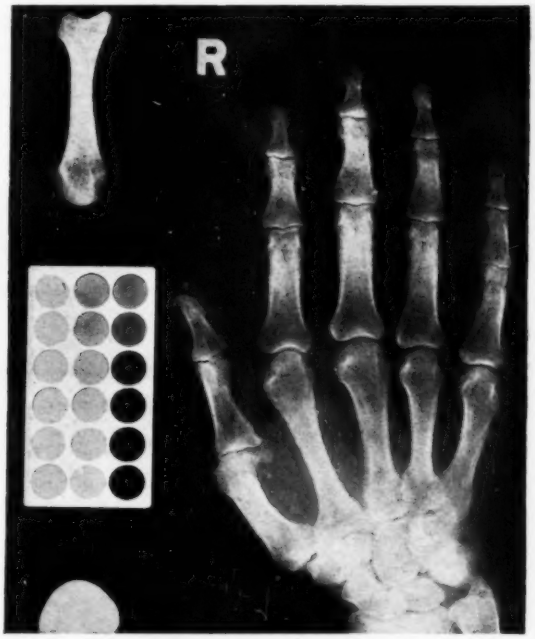


FIG. 4.—Lateral radiograph of chest. August, 1957. Arrows indicate the collapsed vertebrae.



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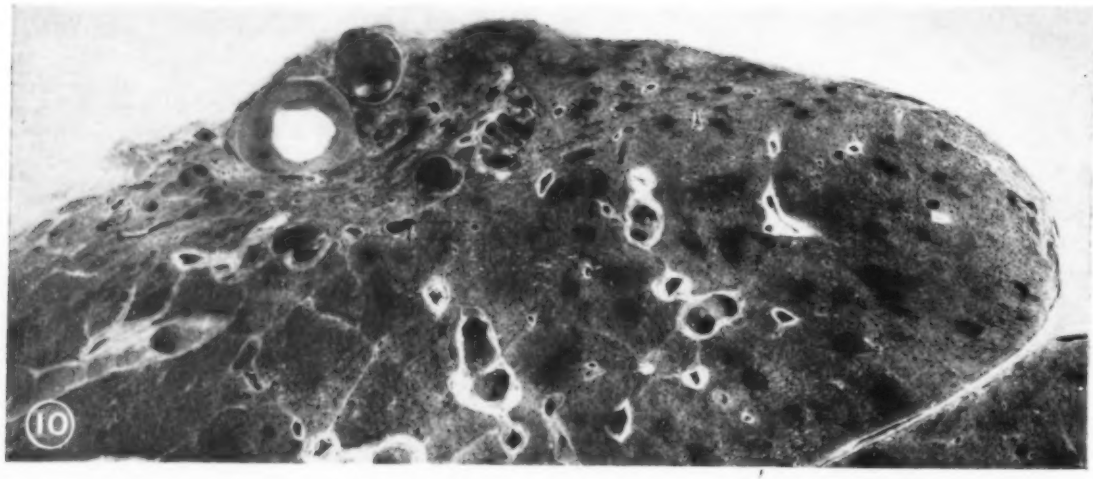

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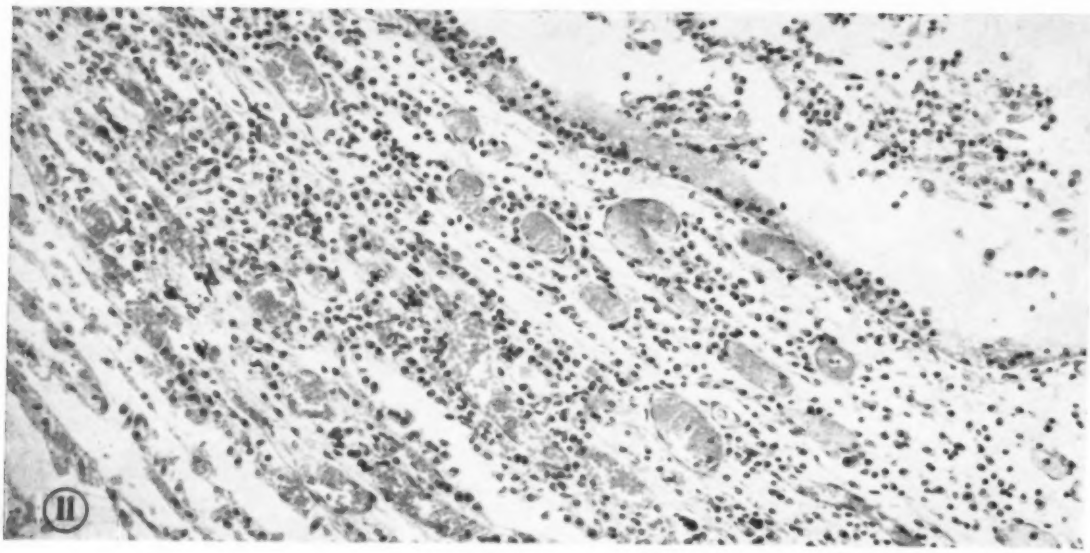

(11)

unaltered and a diagnosis of bronchiectasis was made. He was instructed in postural drainage, and given a fortnight's course of penicillin injections. He improved slightly, but *Haemophilus influenzae* was cultured from the sputum and tetracycline (1 g. daily) was given for a week. His sputum became mucoid and reduced in volume and his shortness of breath decreased. The *x*-ray shadows cleared considerably and he returned to work. He remained fairly well but his sputum repeatedly became purulent, but became mucoid after further short courses of tetracycline in March and June, 1955. From September, 1955, to April, 1956, he was given 0.25 g. tetracycline twice daily. It was then stopped because a resistant *Klebsiella pneumoniae* predominated in his sputum. He remained at work even in foggy weather, but his sputum, though smaller in amount, remained purulent. An estimation of his indirect maximum breathing capacity (M.B.C.) in September, 1955, was 60 litres/min. (normal 64–122). He was able to walk as far as he liked on the level, but was breathless on hurrying.

In January, 1957, he had an episode of acute breathlessness with increased sputum. His own doctor gave him tetracycline and he improved. After this, apical shadows were noted on his chest radiograph (Fig. 3) in both posterior segments. These shadows increased in intensity over the next six months, but seven sputa were negative for acid-fast bacilli. The shadows were probably due to bronchiectasis developing in the upper lobes. Continuous tetracycline therapy was given again, the dose being restricted to 0.25 g. twice daily as before because a larger dose caused diarrhoea.

In May, 1957, the patient was more breathless and he noticed he was getting more round-shouldered. This was confirmed clinically. He developed pain in his shoulders and hypochondrium which was worse on breathing or coughing. He had lost 4 lb. (1.8 kg.) in one month. He was much more breathless and unable to work. A radiograph (Fig. 4) showed very thin vertebrae with collapse of D5, 6, 7, and 9. He was admitted to the Metabolic Unit under Professor T. Russell Fraser.

INVESTIGATIONS

Skeletal.—Further skeletal radiograph (Fig. 5) showed widespread osteoporosis.

Cardiovascular.—Electrocardiograph tracing normal.

Serum.—Calcium, 5.3; phosphorus, 2.1 mEq/litre; alkaline phosphatase, 8.0 K.-A. units; acid formol stable, 1.4 units.

Calcium Balance.—Diet, 15.2; faeces, 12.2; urine 10.8 mEq/24 hours.

Iliac Crest Biopsy.—Osteoporosis. Seams up to 5μ thick.

Strontium Test of Bone Uptake.—Ca_E, 12.7; Ca_B, 2.15 (high normal).

Ventilatory Function.*—F.E.V., 1.04 litres (normal 8–3.5). V.C., 1.61 litres (normal 2.9–3.9). Indirect M.B.C. 36 litres/min. (normal 64–122). F.E.V.%V.C. 64% (normal). No response to isoprenaline. These tests show severe restriction of ventilatory capacity of the restrictive rather than obstructive type, since 64% of the ventilatory capacity was exhaled in 1 second.

SUBSEQUENT COURSE

On discharge, a 600-mg. testosterone implant was given together with 95 mE calcium, 1 mg. stilboestrol, and 0.5 g. tetracycline daily. A spinal brace was fitted but the patient found it too heavy to wear. During the winter the tetracycline was changed to chloramphenicol, 0.25 mg. twice daily, and this kept his sputum mucoid. His breathlessness remained severe and was present even at rest. Oedema of the ankles developed but was thought to be due to varicose veins. On discontinuing chloramphenicol in March, 1958, the sputum soon became purulent and he had great difficulty in coughing because of increasing kyphosis.

In May, 1958, he was readmitted. He was very breathless but not definitely cyanosed. The kyphosis was more extreme, his lower ribs resting on his iliac crest (Figs. 6 and 7). The jugular venous pulse was difficult to see because of his kyphosis, but did not appear to be raised. There was no clubbing. The day after admission he suddenly became cyanosed and comatose. The head of the bed was lowered, a large quantity of purulent sputum was aspirated, but the patient died in 10 minutes.

Clinical Diagnosis

(1) The persistent and profuse purulent sputum was attributed to bronchiectasis affecting both lower lobes at first, and later the upper lobes on both sides.

(2) The kyphosis was due to an unexplained osteoporosis.

A diagnosis of emphysema was made in two radiological reports and it appears in several letters to doctors and on the case notes after his first admission. I do not accept the radiological diagnosis, and the ventilatory function tests were not characteristic of emphysema. I do not believe there was significant anatomical emphysema. The breathlessness was due partly to bronchial obstruction by excessive secretion, but chiefly to the restrictive effect of the kyphosis, and his death was due to suffocation from bronchial secretion which he could not expectorate.

The only evidence of right heart failure was ankle oedema, but he had varicose veins. He was never grossly cyanosed and his E.C.G. was normal. I do not diagnose significant abnormality of the heart.

LEGENDS TO SPECIAL PLATE

FIG. 8.—An antero-posterior slice of the right lung. The upper lobe is flattened by the chest-wall deformity. There is bronchiectasis in many parts, most obvious in the middle lobe and the basal segments of the lower lobe. (Prepared by pressure-fixation and barium sulphate impregnation.)

FIG. 9.—A higher magnification of the middle lobe to show bronchiectasis to advantage. (×1 5.)

FIG. 10.—The apical segment of the right upper lobe is shrunken and bronchiectatic. The black foci in the posterior segment of the upper lobe are centrilobular emphysema. In the shrunken segment, they also have shrunk. (Natural size.)

FIG. 11.—The wall of a small bronchus from the posterior basal segment. It showed bronchiectasis macroscopically. Microscopically the wall is heavily infiltrated by lymphocytes, plasma cells, and some neutrophils, and the vessels are engorged with blood. (×212.)

*F.E.V.$_{1.5}$ = Forced expiratory volume. V.C. = Vital capacity. F.E.V.%V.C. = Forced expiratory volume as percentage of vital capacity. M.B.C. = Maximum breathing capacity. (See Thomson, W. B., and Hugh-Jones, P., *Brit. med. J.*, 1958, **1**, 1093.)

Post-mortem Findings

Dr. B. E. HEARD: The body was thin and there was a marked dorsal kyphosis. The sternum was depressed and the lower costal cartilages projected forwards prominently. The skin of the upper abdomen was creased. There was no clubbing of the fingers.

The *trachea* contained a little yellow mucus. Both pleural sacs were obliterated by adhesions. The *left lung* showed shrinkage and cystic change of the apical and posterior segments of the upper lobe and dilatation of the supplying bronchus. There was bronchiectasis in the lower lingular and posterior basal segments, where bronchi up to 0.8 cm. in diameter reached to within 0.5 cm. of the pleura. The lung was oedematous and congested and showed patches of bronchopneumonia. The *right lung* was prepared by pressure-fixation and barium sulphate impregnation. Fig. 8 shows that the shape of the lung has been altered by the severe kyphoscoliosis. The apical segment of the upper lobe is flattened, the middle part of the lung is ballooned out, and the lower lobe is shrunken. Bronchopneumonia was present and there was bronchiectasis of the middle lobe and most of the lower lobe bronchi. In Fig. 9 the bronchiectasis is shown in detail, sacculations increasing in size as the bronchus is traced distally. In Fig. 10 the flattened apical segment of the upper lobe is shown in more detail. The shrunken zone shows bronchiectasis and solid lung between. The black foci in the posterior segment of the upper lobe are centrilobular emphysema, and it is interesting to note that in the shrunken parts the black emphysematous foci are also shrunken. A section of the main upper-lobe bronchus showed a trace of goblet-cell hyperplasia but no inflammatory changes in the submucosa. Sections of the dilated bronchi of the lower lobe showed heavy infiltration of the whole wall of each bronchus by lymphocytes and plasma cells and destruction of some mucous glands (Fig. 11). Section of the area of apical collapse showed evidence of old carnification but no sign of active tuberculous inflammation.

The *heart* was displaced to the right beyond the costal cartilages and presented through the incision. No abnormalities were noted in the valves or muscle. The right ventricle was of normal thickness. *Coronary arteries* showed an occasional small plaque of atherosclerosis. The *aorta* showed very mild atherosclerosis. About 10 cm. below the arch there was a kink in the aortic wall, probably produced by the vertebral deformity.

The *liver* (1070 g.) was slightly reduced in size and distorted by pressure from the costal cartilages. There were prominent cough-furrows and the cut surface showed centrilobular congestion. Both *kidneys* were normal, but the *prostate* contained a nodule of hyperplastic smooth-muscle 1 cm. in diameter. The *spleen* showed thickening of the capsule and trabeculae. The bone-marrow was red in all the usual sites. The *lymph nodes* at the pulmonary hila were enlarged and oedematous and histologically showed moderate infiltration by neutrophils. The left *testis* was normal; the right showed some parenchymal pallor. Histologically there was atrophy of many of the seminiferous tubules with hyalinization. Leydig cells were very scarce, presumably owing to testosterone therapy.

The *brain* was not examined (permission refused).

The *mid-thoracic vertebrae* were collapsed and some of the *ribs* were fractured. The 6th rib showed a healing fracture which was seen histologically to be united by an adequate amount of woven bone containing small islands of cartilage. The sternum was of a rubbery consistence and easily indented with the finger-tips. Histologically all bones showed osteoporosis with moderate osteoclastic activity unaccompanied by the formation of fibrous tissue. The only fibrous tissue found in the marrow was at small fracture sites in collapsed thoracic vertebrae. The *thyroid* appeared normal, as did the *suprarenals*. The *parathyroids* were dissected out. Histologically there were large islands of pale oxyphils, a not uncommon finding at this age. The fat content was reduced, suggesting slight hyperplasia.

Pathologist's Diagnosis

(1) Idiopathic osteoporosis with severe kyphoscoliosis.
(2) Bronchiectasis and terminal bronchopneumonia.

Discussion

Dr. FLETCHER: There are two aspects of this case: the kyphosis, which I shall leave Professor Fraser to discuss, was the main cause of his death; and the bronchiectasis, which played an important contributory role. I do not quite know what would happen to a man with normal lungs with this degree of rapidly advancing kyphosis, but I think he probably would survive. We know that people with very severe kyphoscoliosis ultimately tend to hypoventilate and go into respiratory failure. In our patient the kyphosis was very acute, causing severe impairment of ventilatory capacity. Death was due to his kyphosis preventing him from expectorating the profuse sputum coming from his bronchiectasis.

BRONCHIECTASIS AND MAINTENANCE CHEMOTHERAPY

The history is a little unusual. He was fairly reliable and he denied cough or sputum before his illness in 1954. He very likely did have a smoker's cough, for he had been a heavy smoker. He sensibly gave up smoking when he first got ill. I think that he already had bronchiectasis when he was first seen; this was four months after the onset of his illness, which may have been a pneumonia which left him with infected basal bronchiectasis. This subsequently spread to involve the upper lobes. We know that bronchiectasis can extend to previously unaffected lung in adults. This has been clearly shown at lobectomy for local bronchiectasis, especially in subjects with pre-operative evidence of generalized bronchitis.

I should like to say something about his management by chemotherapy. He was given no chemotherapy until 18 months after the onset of his illness. In the light of our present experience, it is conceivable that, if he had been vigorously treated from the onset, he would have remained with relatively undamaged lungs. When I first saw him we were not accustomed to giving long-term maintenance chemotherapy. He was given only a week's course of tetracycline, which was then our custom. This was temporarily effective, but he continually relapsed. When we did start maintenance chemotherapy with tetracycline, we were prevented from giving full dosage by the fact that he got

diarrhoea. This, of course, is an annoying side-effect of tetracycline, which we encounter in something like 10–15% of our cases. It usually can be controlled by a simple opium mixture and very often does not persist. Later on we were forced to take the risk of maintenance on chloramphenicol, which was much more effective, but the bronchial infection relapsed as soon as it was discontinued.

Professor J. McMICHAEL: Two questions. When he came in last no clinical cyanosis was noted. Did we have an arterial sample?

Dr. FLETCHER: No. He died within a day.

Professor McMICHAEL: Was he never grossly cyanotic?

Dr. FLETCHER: There are occasional out-patient notes of slight cyanosis, but he was never grossly cyanotic.

Professor McMICHAEL: What was the cardiac state?

Dr. FLETCHER: It seems to have been normal. There was no evidence of right hypertrophy. I do not think his ankle oedema was cardiac.

PROGRESSIVE OSTEOPOROSIS

Professor T. RUSSELL FRASER: Well, this is an instance of osteoporosis, unfortunately a condition which is not very well understood nor very easy to treat. But I suspect that his disorder must have been more severe than is usual in men, and perhaps more difficult to treat because of his associated cough. It is at least not at all common to see a progressive kyphosis advancing as rapidly as that. How much the cough contributed to it is hard to say. From the fact that he had osteoporotic bones in the radiological meaning of the term we can infer that the man must already have lost over 50% of his bone mass. If there is, in addition, the mechanical problem of coughing, I suppose progression may almost be inevitable.

The normal treatment would include a spinal brace to place the support of his shoulders on to his iliac crest; but doubtless he could not manage with his brace, since it must have increased his dyspnoea very considerably. On the other hand, progressive collapse was probably inevitable without it; for even with the best response to the conventional methods of treatment osteoporotics can only be made to recalcify slowly.

The diagnosis of osteoporosis, like that of emphysema, is made by exclusion of other causes. Here the data have shown that there was no evidence of osteomalacia or hyperparathyroidism; especially from the normal serum electrolytes—particularly the serum calcium, phosphorus, alkaline phosphatase.

Professor McMICHAEL: What were the figures?

Professor RUSSELL FRASER: The calcium balance can be interpreted only in the light of the dietary intake. These balance figures are all given in mEq per 24 hours when he was on a diet of 15.2 mEq (or 304 mg.) of calcium per day. His faecal loss was 12.2 mEq calcium/24 hours and his urine loss was 10.8. So he was obviously in abnormally strong, negative calcium-balance (−7.2 mEq/24 hours); though that does not tell you anything about the nature of the decalcifying process.

Professor McMICHAEL: Is this characteristic of osteoporosis?

Professor RUSSELL FRASER: In osteoporosis it is a matter of whether the disease is advancing and active at the time when you do the test, or has become quiescent and stationary. Very often the patient is seen at this last stage when you would not see a negative calcium-balance. But of course it should be said that a negative calcium-balance is a normal finding on that dietary intake. This particular patient was balanced on a low normal calcium-intake, chosen as the diet on which the faecal calcium and the dietary intake are approximately equivalent. He was also balanced later on a high calcium-intake when he went into positive calcium-balance It is a very frivolous custom, therefore, to talk about somebody being in negative calcium-balance on a test, or in positive calcium-balance, for this really means nothing unless you relate it very carefully to his dietary intake and whether that is what his usual diet is. The only abnormality in this patient's balance data is that he had a high urinary calcium. The rest of the data, the faecal loss, was probably normal. His serum levels were also normal (serum levels of calcium, phosphorus. and phosphatase), and that is the reason for concluding that he had shown no primary defect of calcium metabolism.

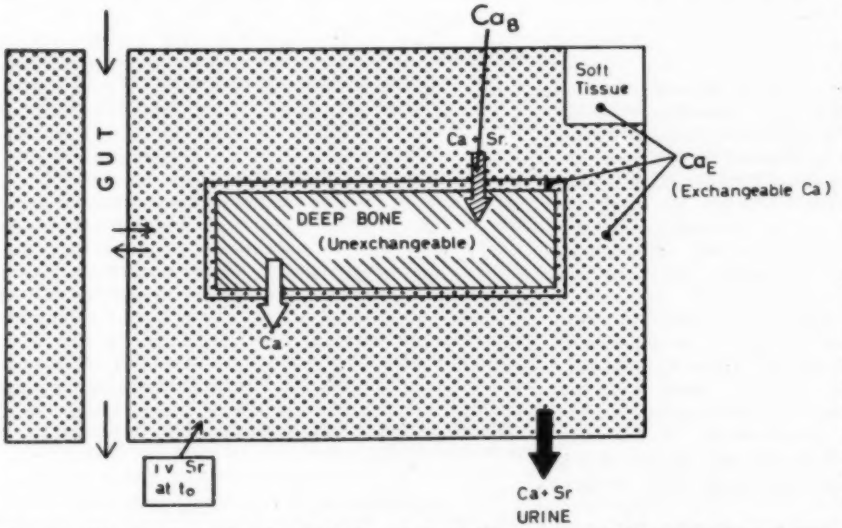

FIG. 12.—Diagram illustrating the distribution of the body's calcium and the strontium tracer test.

STRONTIUM UPTAKE TEST

Professor McMICHAEL: I am sure about half of the people here, Professor Fraser, do not know about the strontium test for bone uptake. The figures are here in the record and we should be very glad if you could explain them.

Professor RUSSELL FRASER: Well, it is possible to use strontium, somewhat in the same way as radio-iodine is used, to measure the rate of calcium uptake in the bones. From a pool in the body fluids, calcium goes to two main external sites, the urine and the faeces, and it goes also to the bones (see Fig. 12). The pool is replenished from the absorbed dietary calcium and also from the steady resorption of bones. Now, with an injection of strontium—or for that matter of any tracer of calcium—into the body fluid's pool of calcium, you can measure the rate at which calcium disappears from the pool, and also the rate at which it is excreted into the urine and the faeces. The loss not so accounted is therefore the uptake of calcium by the bones. The test is primarily concerned with measuring the size of the bone uptake. The statement that this patient had a normal uptake means that he did not show any signs of an excessively rapid turnover of calcium through the bones. Such a rapid bone turnover is found when you have primary overaction of the parathyroid, and it is also a finding in osteomalacia, in which, for perhaps rather more complex reasons, the bones similarly have a very rapid turnover of such calcium as the body can offer, the defect perhaps being primarily in the absorption of calcium.

Professor MCMICHAEL: Now your answer is expressed here as Ca_E, 12.7; Ca_B, 2.15. What does that mean?

Professor RUSSELL FRASER: Well, calcium E is the exchangeable calcium mass, that is what is illustrated in the diagram as the pool of calcium into which an injection is rapidly mixed. That is compounded of the plasma, the extracellular fluids, soft tissues, and the surface of the bone. The units are "total plasma" units. These rather unusual units are needed because you have to incorporate a correction for body size. A Ca_E of 12.7 means that he had 12.7 times as much calcium in the exchangeable pool as he had in his plasma. The normal figures for this are 10–15. Now Ca_B, shown by an arrow on the diagram, is the calcium deposited in bone each day. And that again is expressed in plasma units. The test showed that he deposited 2.15 plasma contents per day, and the normal range for this being 0.8–2 plasma units he was therefore at the upper end of normal. You might expect simple osteoporosis to show defective laying down of bone by this test, but it is interesting that this has not been our experience. In fact, the results in osteoporosis have been remarkably similar to those in normals. We must, however, think carefully what is to be concluded from that. Let us compare the situation in, shall we say, obesity. Nobody really doubts that the obese patient eats a little more than he needs for the energy he expends, but if you attempted to demonstrate this on a metabolic test it would be very difficult. It probably takes many years to develop osteoporosis, just as it takes many years to develop obesity, and our tests are not sufficiently sensitive to show that this little arrow has perhaps been reduced over a very long period of time. The important diagnostic feature is that the uptake is not increased, as it is in those two other conditions which may readily be confused clinically—hyperparathyroidism and osteomalacia.

Dr. M. D. MILNE: Isn't it very odd, though, that in a very active case it was right at the upper limit of normal?

Professor RUSSELL FRASER: I think it's very probable that, when we discover what osteoporosis is due to, we will find it isn't the conventional explanation that the bones do not lay down matrix normally and so lay down insufficient bone; there is a chronic excessive loss of calcium from the body and so it may well be that excessive resorption is the explanation. Certainly that is, for example, the case in thyrotoxicosis, where you may ultimately get an identical clinical picture of thin bones as a part of the syndrome in a proportion of the patients. But when you examine these or other thyrotoxics bone deposition is found to be rapid and excessive; however, it is not so great as bone resorption, and it is the balance between these two which will determine whether the bones end up as being thin.

Professor MCMICHAEL: Has Nordin's theory of osteoporosis resulting from defective absorption been accepted?

Professor RUSSELL FRASER: No, not generally accepted yet. You can produce the disorder of osteoporosis by a low-calcium diet in rats. Osteoporosis results if you give them a low dietary intake of calcium, along with otherwise adequate diets. So this is one way of producing atrophy of the bones, which is what we are talking about. Osteoporosis is an atrophy of the bones without any indication of the cause of the atrophy, and there may be several causes of the bone atrophy. When we come to the question of the osteoporosis seen clinically, we have no adequate clues yet. Calcium deficiency could cause it, but this has not been shown to be the cause. Calcium therapy is being tried. Defective bone formation is still a possible cause, for with thin bones there would be an excessive stimulus to calcium deposition, yet all these patients achieve is a normal rate of deposition. You may say that is abnormal.

HOW BRONCHIECTASIS SPREADS

Dr. J. G. SCADDING: I agree with Dr. Heard's analysis of the situation rather more than with Dr. Fletcher's. As I understood it, what Dr. Heard suggested was that the primary event here was the development of a bronchitis of the truly inflammatory type. I agree with him that the first event here was a succession of purulent infections of the bronchi and that the bronchiectasis developed as a consequence. As I saw it, what Fletcher was suggesting was that a local bronchiectasis developed somewhere as a result of an acute pneumonic episode and the bronchiectasis "spread" from that focus. Admittedly, bronchiectasis may appear to spread in the lungs, but I think that the word "spread" is rather an unfortunate way of expressing it. It rather suggests that bronchiectasis is a little demon that goes about dilating people's bronchi. My thought is that, when bronchiectasis appears to spread, it is certainly a repetition of the process that caused the original bronchiectasis: another focus of a similar inflammatory change occurs in another part of the lung and bronchiectasis develops there. I think the bronchiectatic changes observed finally at the post-mortem examination in this case were of a distribution which suggests that Dr. Heard's explanation—that mainly they were a consequence of chronic and recurrent widespread inflammatory changes in the bronchi—is probably correct.

EMPHYSEMA NOT A CLINICAL SYNDROME

The really unusual feature of this case, to my mind, from a pathological point of view, is the extremely

small amount of emphysema that was in evidence at the end of the process. I would have expected, in a case where all these changes had been going on for so many years, a good deal more emphysema. I was very glad to hear pin-pointed the difficulties over the diagnosis of emphysema. We are trying to establish the idea that the only tenable definition of emphysema is a morbid anatomical one, so that the only person who can say for certain whether emphysema is present is the morbid anatomist. When, as clinicians, we are bold enough to say, "I think this patient has emphysema," what we should mean is that we think that the morbid anatomist will find certain morbid anatomical changes. We may be wrong or we may be right, but that is what we should mean. Unfortunately the word "emphysema" has become one of those witchwords which misleads everybody, because it has become equated with a clinical syndrome without any real justification. Indeed, I think this happens all over the world; certainly it happens in the United States. Recently I received, from a centre in the United States for the journal which I edit, a paper in which a case report recorded that the patient had had "recurrent attacks of emphysema." This makes clear that the word emphysema is used by some people there in the same sense in which most of us in this country refer to recurrent or chronic bronchitis. I don't think we'll overcome this confusion until we can get it established that ultimately emphysema is a morbid anatomical concept.

What we urgently need is a convenient word to describe the syndrome of chronic respiratory disease leading up to eventual respiratory insufficiency, which is so common in this country, without necessarily implying any untenable hypothesis. The position in respiratory disease at present, with the current use of the word emphysema, is rather similar to that which would exist in cardiology if you could not refer to "cardiac failure" without implying that there was valvular disease of the heart. We want functional terms in respiratory disease that would be as commonly used and understood by everybody as "congestive cardiac failure" is in cardiology. Having introduced that term into our respiratory work, we could then go on to add, to complete a diagnosis, the morbid anatomical changes among which might be emphysema.

A VOICE: What about "respiratory failure"?

Dr. SCADDING: Well, that would be a nice term to use, but unfortunately it's not quite precise enough. "Respiratory failure" might imply failure of the respiratory centre as well as of the lungs. "Pulmonary insufficiency" is the nearest I can get to it, implying a local insufficiency in the lungs.

Dr. FLETCHER: I should just like to say that I do not look on bronchiectasis as a demon. I entirely agree with Dr. Scadding that its spread is due to extension of infection with destructive results, but I do not think this case was one of bronchitis in the ordinary sense, because we do not see this process in most of our bronchitics. There was something different about this bronchitis. Did Dr. Heard say that he did not find hyperplasia of mucus-secreting glands in the bronchi? In my mind bronchitis is characterized primarily by goblet-cell and mucous gland hypersecretion. In this case there was no real history of chronic bronchitis preceding the first illness. There was a rapidly progressive bronchiectasis starting, I believe, with an acute infection. Later on bronchiectasis developed elsewhere, so that some processs was spreading in his lungs which had as a secondary consequence bronchiectasis. This may have been a peculiar kind of bronchitis, but it was not the ordinary kind in which there is persistent mucoid sputum with recurrent episodes of infection. This man had a persistently purulent sputum and radiological evidence of bronchiectasis at first in the lower lobes and subsequently in the upper lobes.

EFFECT OF THE KYPHOSIS

Dr. R. E. STEINER: The appearance of lesions in the upper lobes coincided with the kyphosis.

Dr. FLETCHER: Yes, they appeared in January, 1957, when the P.-A. radiograph shows increased kyphosis, but this wasn't noticed clinically till about four months later. Do you suggest that he had a collapse of his upper lobe and got a secondary infection in it, which may have led to the bronchiectasis?

Dr. STEINER: Yes, the mechanical compression was the first thing, at least in the case of the upper lobes. You are not dealing with a primary infection of the bronchi, on which you base your explanation of the bronchiectasis.

Dr. P. C. ELMES: I wonder which was causing the lung disease, the vertebral collapse or the bronchial infection? The disease process may have been primarily a bronchial infection, perhaps associated with some other pulmonary disease. He was coughing up about 200 ml. of purulent sputum per day, containing 10% of protein, for many years, and his disease was associated with anorexia. Thus protein deficiency could have occurred and given rise to bone absorption with vertebral collapse and progressive symptoms. This in turn made it impossible for us to clear his lungs of infection. Two processes were going on at the same time and you never could say which came on first, or which was the more important; they added to each other all the time. I wonder whether the final picture of minimal emphysema was due to the fact that here were lungs which were getting progressively scarred but were not being asked to occupy the normal space. Had they been asked to occupy the normal 5 or 6 litres of thoracic volume, then there would have been very much more likelihood of emphysema because the lungs would have been stretched to fill that large volume, whereas because of the collapse they were not being stretched at all.

Professor MCMICHAEL: Isn't it rather unusual, Dr. Heard, to see completely collapsed segments of the lung in these deformed hunchbacks? My observation of the ordinary kyphoscoliotic is that the lungs are small but otherwise normal.

Dr. HEARD: Complete collapse is unusual, but some shrinkage is not uncommon with deformities of the chest wall or with pleural thickening. The defect is not always one of compression. We have had a few cases of severe kyphoscoliosis recently. One of them was a man of 53 who developed kyphoscoliosis early in childhood. He had very small lower lobes to both lungs. The defect was not so much due to compression by the deformity, but to the fact that his lungs appeared never to have developed to the normal size. Incidentally, he had no bronchiectasis and no emphysema was demonstrable though the lungs were prepared by pressure-fixation and barium sulphate impregnation.* As regards the bronchial histology in the present case,

* Heard, B. E., *Thorax*, 1958, **13**, 136; ibid., 1959, **14**, 58.

the small bronchus showing marked goblet-cell hyperplasia was of the sort described by Reid.*

We are grateful to Dr. J. P. Shillingford and Dr. B. E. Heard for assistance in preparing this report, and to the photographic department of the Postgraduate Medical School for the illustrations.

EXTRACTS AND HOWLERS TAKEN FROM EXAMINATION SCRIPTS

BY

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The following are authentic extracts from examination papers collected through the years by the senior sister tutor of a well-known hospital.

Anatomy

Wax glands in the ear protect the organ from foreigners.

The pupil is nothing more than a whole in the eye. In some people it is big, in others small, but unless you have been peculiarly born it is there in some size or another.

The stomach is covered with a serious membrane.

The stomach is supplied by an involuntary nerve called the pneumatic.

The aorta is a long tub whose contents are very precious to the body.

The eye is the organ of site, the sight of which is in a holler in the temple.

At the back of the eye one may see a retinue.

The heart is the only organ in the body made of heart muscle.

The heart is a muscular organ acting like a human pump, which pumps the heart around the body at regular intervals.

The heart is an organ the shape of a heart. It is not quite heart shaped because there are tubes protruding from it, 4 from top left, an umbrella handle from bottom left, a "Y" shaped connection from bottom right and 2 tubes from top right.

The brain will soon become a weekend one.

At the back of the throat are 2 long pillars of faeces.

The mouth is situated in the lower part of the face and is known as a buckled cavity.

Personal and Communal Health

The best room for eye trouble is one which is well alight.

The shopkeeper should thoroughly rap all cakes before selling them to make sure all disease is eliminated.

Food should not be picked up by hand but with tongues.

Clean overalls or trousers should be worn to polish the fruit on.

These are some of the types that help in hygiene of the country: (1) Road sweepers. (2) Dustmen. (3) Nurses in the district and so on. All these add up to the answer prevention of spread.

If blue bottles come through the larder window trouble is around.

Cooks should be trained to wash their hands after a visit to the toilet it is through wiping them on food that diseases are spread.

Overcrowding is not necessary. People when they get married their parents say they can live with them until they get a house built. Some people think, well as long as we can live with them it is all right. BUT IT IS NOT. After they have been married a few months they start having children, these grow up and this goes on. Overcrowding then occurs air is not allowed to enter, with too many in the bed diseases are caught. Conditions like this can be likened to the many hundreds of people who were put in a black hole in Calcutta and burried alive.

Rest is essential if habits are to be good ones, if you do not rest then habits will be bad ones, so proper rest and good cleaning of the body will produce a nurse who can be relied upon to perform any old job the sister may have on her list.

Our Tutor has stated that in her opinion all infection in hospitals is caused by dirty nurses, therefore personal hygiene and cleanliness is next to godliness, and is the first thing to remember if you want to prevent wounds from becoming pussy.

The important thing in the maintenance of health is personal cleanliness. This commences when the person is getting up in the morning, and it continues until the person is ready for getting up again.

You always find a person who does not practice personal cleanliness is not nice to be near.

Everything about personal cleanliness should be kept very clean, making sure that the habits are not forgotten.

The body needs a daily inspection to make sure every part is in proper working order.

The teeth should be brushed with a brush and toothpaste. The best method is to have 2 brushes and keep one of them in a septic solution.

Clothes should be well washed and ironed for hygienic conditions and also for decorating purposes.

In bad light people may screw up their eyes and the damage they do may never be undone.

Housewives when baking should wear the appropriate head gear.

Flies may land on composed heaps then pass through a crack in a house, settle on persons within and cause trouble amongst them. Few escape this vital pest.

Flies spread disease "you can say that again."

Food should be kept covered in shops because of the diseased types who buy it.

If overcrowding continues water vapour increases and people will shout for air, this when heard denotes air hunger.

We seek them here, we seek them there, we seek those horrid flies everywhere.

Flies are abundant wherever rubbish, manure, filth and hospital food are found.

Flies may be shot down whilst in flight by the aid of D.D.T. bombs.

If open shoes are worn on duty the toe nails should be kept clean and short as they are on view to all the patients.

Curt shoes and swede shoes are generally baned by the Matron.

A nurse has no choice in the footwear she wears, the Matron chooses her shoes for her.

The ear is the organ of earing.

Nursing

Treatment of Shock

The best treatment is to rape the patient in old blankets making sure she is not overheated.

The woman should have blankets under and over her but onlookers must be kept outside.

Coronary Thrombosis

The severity of the attack depends upon the sight of the clot.

The patient must adhere closely to the bed rest.

Common Cold

The common cold is caused by an organism called droplet bacillus.

The patient will suffer from a steaming nose.

*Reid, L. M., *Lancet*, 1954, **1**, 275.

Fractures

If compound titanic serum is given.

For fractured beck of femur plaster of Paris is applied from the head to the foot.

In chronic nephritis a director is given to the patient to make her pass more urine.

To clear sputum posterior drainage is carried out three times a day.

Acute Bronchitis

If the patient coughs he is very likely to become a little horse.

THE LOTOS-EATERS, OR STRESS, NEUROSIS, AND TRANQUILLIZERS

BY

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Surely, surely, slumber is more sweet than toil, the shore
Than labour in the deep mid-ocean, wind and wave and oar;
O rest ye, brother mariners, we will not wander more.

TENNYSON.

It is fashionable to assert that the stress to which we are subject is increasing, that this is causing a greater incidence of nervous disorders, and that tranquillizers are desirable for the "restlessness and anxiety of modern man." It is very doubtful whether any of these beliefs are true; certainly no scientific evidence has been produced to substantiate them.

Stress

It is difficult to define qualitatively or to measure quantitatively what might be called a pathological stressful event or situation. What is stressful for one person may be quite innocuous for another. A mouse or a spider may induce an acute state of stress in one human being while leaving another totally indifferent. A serious recession in Wall Street may cause such stress to a loser that he reacts by hurling himself from the twentieth story of a skyscraper; but many other losers react in much milder fashion. Whether a stressful situation produces a pathological reaction will depend on the vulnerability of the personality concerned, and there is nothing to prove that the human species has become less tough. As for the stresses of life, these are much the same as they always were, and are related to problems of food, shelter, disease, love, and the desire for prestige or power. There is no reason to believe that thwarted love, the pangs of hunger, or the loss of freedom are more poignant or more frequent to-day than they were in Assyria and Babylonia, Greece and Rome, in the Middle Ages, or during the nineteenth century. Indeed, many stressful factors have diminished both in frequency and in intensity. During the past fifty years wages and the general standard of living have risen; in many trades and professions there are paid holidays and pensions on retirement; there are sickness and compensation benefits, old-age pensions, national assistance, better housing, and so forth. The stresses caused by poverty, unemployment, disease, and insecurity have been considerably lessened.

The "rapid tempo of modern life" is often blamed for the alleged increase of mental disorders, but it is not clear why crossing the ocean comfortably by aeroplane in a few hours should be more stressful than being seasick on a schooner which may roll and pitch for several weeks, or why travelling in an express train should be worse for the nerves than being rattled in a horsedrawn chaise over a track of ruts and potholes, with the added chance of being waylaid by a highwayman. I suppose that when the first wheel was invented, someone exclaimed: "This new terrible pace of life on wheels will surely ruin us all." It is perhaps of some significance that quite a number of adventurous people attempt earlier forms of transport—for example, crossing the seas in a ketch or on a primitive raft. Are they seeking stressful situations because they are bored by the excessive ease and comfort of modern life? It may be that many of us really need more, not less stress.

Neurosis

Admissions to mental hospitals in England and Wales more than quadrupled between 1920 (over 21,000) and 1957 (over 89,000), but this does not mean that mental illness has become four times as frequent. In 1920 only the cases severe enough to be certified could be admitted, whereas now the earlier and milder psychoses, the neuroses, a host of psychosomatic disorders, the psychopathies, are being admitted—types which had always existed. There are so many difficulties in assessing the incidence of neurosis that it is impossible to give accurate figures which would enable comparison of one era with another, one nation with another, or even different parts of the same country to-day. There is first of all the impossibility of telling where normal ends and abnormal begins.

If a normal person is defined as one who has been psycho-analysed, as has been quite seriously suggested, then very few indeed are normal. According to Freud (Wortis, 1954), "Everybody has some neurotic traits . . . phobias are very common, and I have had three or four myself." Ernest Jones (1955) thinks that many of Freud's psychosomatic complaints—for example, indigestion, constipation—were symptoms of a neurosis. But, of course, Freud did not appear in out-patient statistics as a case of neurosis, and there must be numerous lesser men with phobias and psychosomatic disturbances who are or are not counted for a variety of reasons. A wisecrack is that you are a neurotic if you are foolish enough to get into the hands of a psychiatrist, and this certainly explains the source of most of the statistical information that we possess. However, there are so many variables involved that such numbers have but little significance when studying problems of alterations in incidence. Among such variables are: (1) the prevailing social fashion of when to complain and what to complain about; (2) the pressure of relatives or friends to influence consultation with a doctor; (3) the policy of the general practitioner, both in diagnosing neurosis and in referring to a psychiatrist; and (4) the availability of a psychiatrist, and the variability of his diagnosis.

Undoubtedly many cases of neurosis have been treated, and still are, by general physicians, neurologists, gynaecologists, dermatologists, and other specialists, under the guise of appendicitis, neuritis, endometritis, and dermatitis. It is instructive to read that Freud's obscure disorder, diagnosed as colitis or cholecystitis,

might have been in part a psychosomatic relic of neurosis (Jones, 1955). The incidence of psychological disorders as estimated by general practitioners in their field of work varies greatly. Some give a figure as low as 5%, whilst others—for example, Pasmore (1958)—rate it as high as 40% ; and it is obviously futile to compare with equally varying figures of 50 or 100 years ago, when, moreover, diagnostic categories were different. Altered social conditions and new laws will also influence reported incidence—for example, lack of sick pay compelled some people to carry on with work in spite of a neurosis, and free medical service encourages more frequent consultations. It may be that in the past many people bore neurotic symptoms quietly and stoically, but this does not imply a lesser incidence. The question of increasing incidence is answered impartially by Lemert (1951) as follows: "The history of mental disorders and their treatment in our society leaves us with no incontestable proof that the present-day incidence of these disorders is much greater than in the past, despite the impression created by rapidly growing hospital populations."

Tranquillizers

There is hardly the time to assess with certitude the efficiency of one drug when another appears on the market. A percentage of successes with any new drug exhibited in the neuroses is inevitable for at least two reasons, the influence of suggestion and the fact that the milder neuroses and the minor psychosomatic disturbances are apt to get better with time and with the aid of extraneous factors, such as change of address, acquisition of a new friend, or change of occupation. The "placebo reaction" guarantees relief of symptoms in about 30% of cases. The power of an intensive advertisement campaign may easily double this figure.

Whether chemical or suggestive, or both, tranquillizers have a number of disadvantages. Side-effects such as dry mouth, blurred vision, nausea, drowsiness, occur in a percentage of cases with all of them, and toxic effects such as liver damage, with jaundice or agranulocytosis, are a risk with some. Though few are addictive in the narrow sense, they can all become habit-forming, and withdrawal symptoms have been reported. The most vital objection, however, is that the doctor may use them as a quick way of assuaging the symptoms, instead of trying to cure the illness. The emotional disturbance is damped with a drug instead of its origin being analysed. Though some advertisers are clever enough, after praising the virtues of the new drug, to mention also the necessity of psychotherapy, one wonders how often this is carried out in practice. One cannot expect a busy doctor or a busy patient to sacrifice time in searching for the causes of an anxiety state if a tablet can succeed in dulling or banishing the unpleasant sensations. The liberal use of tranquillizers can thus encourage an evasion of a search for the psychogenic, familial, and social determinants of disease. Problems and conflicts are obscured in a thick cloud of chemically induced tranquillity.

I do not intend to condemn the proper use of tranquillizers, which are finding a useful sphere in psychiatry, particularly in the psychoses, but there is no doubt that they are also much abused. For this a widespread acceptance of the false beliefs mentioned at the beginning of this paper, the flood of advertisements by pharmaceutical firms and the suggestibility of doctors, is responsible. Also the financial drive of pharmaceutical firms cannot be ignored, as Leiberman and Vaughan (1958) have commented: "Tranquillizers are big business." Advertisements claim success not only for the neuroses or anxiety and tension states, but for such conditions as worry, headaches, irritability, nervousness, restlessness, fatigue, apprehension, hostility, excitement, mild emotional disturbances, and so forth. But is there any human being, except when he becomes a corpse, who does not experience such moods or types of behaviour at some time or other in appropriate circumstances? Some firms when listing indications make a show of being more scientific by suggesting a pathological state with the prefix "over" or "hyper"—for example, over-aggressiveness, over-irritability, over-excitability, over-anxiety, hyperactivity, overwork—but there is no indication of what the standard of normality might be or how an excess is to be measured.

What is happening on a large scale is that an enormous cost to the National Health Service is being incurred by the swallowing of millions of tablets whose effect is to dope emotional reactions, which are either within normal limits or are in need of psychotherapeutic investigation with a view to reconditioning the patient's pattern of behaviour or modifying his environment. Indeed, it may also be argued that the persistent doping of anxieties and tensions can retard social progress because the drives towards an amelioration of environmental deficiencies are weakened. The ideal tranquillizer, free of all side-effects and toxic reactions, and non-addictive, may, by dulling our reactions to frustrations and lulling us into inactivity, prove to be more of an evil than a blessing to humanity.

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THE MENTAL HEALTH ACT, 1959

A PRACTITIONERS' GUIDE

[FROM A SPECIAL CORRESPONDENT]

The Mental Health Act* reached the statute book on July 29, 1959, but, owing to the reorganization needed to implement its provisions, it will not come into operation until a date appointed by the Minister of Health. This date is not yet known, but may be in the summer of 1960. However, by Commencement Order No. 1, 1959, hospitals, licensed houses, and nursing-homes may already receive mentally ill patients informally without powers of detention. This early arrangement clearly indicates the Act's emphasis on voluntary, rather than compulsory, treatment.

To the medical practitioner this 154-section Act might seem a formidable production. Fortunately for him, much in it is pure administration, dealing with, for example, guardianship, transfers of patients, and management of property and affairs. Part V, dealing with the disposal of criminals with mental disorder, is long and interesting, but not important to the ordinary practitioner. Less than 20 of

**Mental Health Act, 1959*. H.M.S.O., London. Price 8s. net.

the sections concern medical men directly, and, really, the trend is towards simplification. The general practitioner would be well advised to master Sections 25 to 29 thoroughly.

The theme of the Act is mental disorder as a matter for treatment and not custodianship. The Board of Control is dissolved and its members and officials become officers of the Ministry of Health. Informal, rather than compulsory, treatment is emphasized, and nothing in the Act is to interfere with this principle. When compulsory treatment becomes inevitable there are many safeguards against wrongful detention.

Definitions

Treatment of lunacy and mental deficiency in the past has been governed by a patchwork of statutes, and these are all now repealed, being replaced by the Mental Health Act, 1959. No distinction is made, as regards administration, between psychosis and mental defect, all disorders of the mind coming under the heading of "mental disorder." The oligophrenic groups are "subnormality" and "severe subnormality." A notable innovation is the recognition of the important group of psychopaths, which the Act courageously defines in Section 4(4).

In this Act "psychopathic disorder" means a persistent disorder or disability of mind (whether or not including subnormality of intelligence) which results in abnormally aggressive or seriously irresponsible conduct on the part of the patient, and requires or is susceptible to medical treatment.

Compulsory Admission

The magistrate no longer has any part in the certification of insane persons. This again lays stress on the medical, as opposed to the administrative, outlook on mental disorder. The duly authorized officer takes the name of mental welfare officer, but his duties will, no doubt, remain much the same and he is still appointed by the local authority.

The procedure for compulsory admission to hospital is by application, with the recommendation of two doctors. One doctor must have special psychiatric experience and the other, if possible, previous acquaintance with the patient—obviously the family doctor. The psychiatric practitioner must have been approved by a local health authority as having special experience in the diagnosis or treatment of mental disorder. The criteria are not yet known, but he will probably have consultant, or at least senior registrar, status. This means that everyone seriously mentally ill will be more likely than at present to have the advantage of a psychiatric opinion.

The application for admission is made by the nearest relative if available, otherwise by the mental welfare officer, who again must try to consult a near relative. A safeguard to the public is already apparent here; under the present law a magistrate and any doctor can certify a person as insane.

Compulsory admission is for 28 days for observation. This gives ample time for reaching a diagnosis, or, in many acute psychoses, for recovery. The decision for longer detention can be taken after deliberate assessment and can be extended for yearly periods. An emergency application may be made on the recommendation of one doctor only, and is valid for 72 hours.

Sections on Compulsory Admission

The sections of the Act relating to compulsory admission are here set forth and are worth filing:

Section 25

(2) An application for admission for observation may be made in respect of a patient on the grounds (*a*) that he is suffering from mental disorder of a nature or degree which warrants the detention of the patient in a hospital under observation (with or without other medical treatment) for at least a limited period: and (*b*) that he ought to be so detained in the interests of his own health or safety or with a view to the protection of other persons.

(3) An application for admission for observation shall be founded on the written recommendations in the prescribed form of two medical practitioners, including in each case a statement that in the opinion of the practitioner the conditions set out in paragraphs (*a*) and (*b*) of subsection (2) of this section are complied with.

(4) Subject to the provisions of Section 52 of this Act (in a case where an application is made under that section for transferring the functions of the nearest relative of the patient), a patient admitted to hospital in pursuance of an application for admission for observation may be detained for a period not exceeding 28 days beginning with the day on which he is admitted, but shall not be detained thereafter unless, before the expiration of that period, he has become liable to be detained by virtue of a subsequent application, order or direction under any of the following provisions of this Act.

Section 26

(2) An application for admission for treatment may be made in respect of a patient on the grounds (*a*) that he is suffering from mental disorder, being (i) in the case of a patient of any age, mental illness or severe abnormality; (ii) in the case of a patient under the age of 21 years, psychopathic disorder or subnormality; and that the said disorder is of a nature or degree which warrants the detention of the patient in a hospital for medical treatment under this section; and (*b*) that it is necessary in the interests of the patient's health or safety or for the protection of other persons that the patient should be so detained.

(3) An application for admission for treatment shall be founded on the written recommendations in the prescribed form of two medical practitioners, including in each case a statement that in the opinion of the practitioner the conditions set out in paragraphs (*a*) and (*b*) of subsection (2) of this section are complied with; and each such recommendation shall include (*a*) such particulars as may be prescribed of the grounds for that opinion so far as it relates to the conditions set out in the said paragraph (*a*); and (*b*) a statement of the reasons for that opinion so far as it relates to the conditions set out in the said paragraph (*b*), specifying whether other methods of dealing with the patient are available, and if so why they are not appropriate.

(5) An application for admission for treatment made on the ground that the patient is suffering from psychopathic disorder or subnormality and no other form of mental disorder referred to in subsection (2) of this section, shall state the age of the patient, or, if his exact age is not known to the applicant, shall state (if it be the fact) that the patient is believed to be under the age of 21 years.

Section 27

(1) Subject to the provisions of this section, an application for the admission of a patient for observation or treatment may be made either by the nearest relative of the patient or by a mental welfare officer; and every such application shall be addressed to the managers of the hospital to which admission is sought, and shall specify the qualification of the applicant to make the application.

(2) An application for admission for treatment shall not be made by a mental welfare officer if the nearest relative of the patient has notified that officer, or the local health authority by whom that officer is appointed, that he objects to the application being made, and, without prejudice to the foregoing provision, shall not be made by such an officer except after consultation with the person (if any) appearing to be the nearest relative of the patient unless it appears to that officer that in the circumstances such consultation is not reasonably practicable or would involve unreasonable delay.

(3) No application for admission of a patient shall be made by any person unless that person has personally seen the patient within the period of 14 days ending with the date of the application.

(4) An application for the admission of a patient shall be sufficient if the recommendations on which it is founded are given either as separate recommendations, each signed by a medical practitioner, or as a joint recommendation signed by two such practitioners.

Section 28

(1) The recommendations required for the purposes of an application for the admission of a patient under this part of this Act (in this Act referred to as "medical recommendations") shall be signed on or before the date of the application, and shall be given by practitioners who have personally examined the patient either together or at an interval of not more than seven days.

(2) Of the medical recommendations given for the purposes of any such application, one shall be given by a practitioner approved for the purposes of this section by a local health authority as having special experience in the diagnosis or treatment of mental disorder; and, unless that practitioner has previous acquaintance

with the patient, the other such recommendation shall, if practicable, be given by a medical practitioner who has such previous acquaintance.

(3) Where the application is for the admission of the patient to a hospital not being a mental nursing-home, one (but not more than one) of the medical recommendations may be given by a practitioner on the staff of that hospital, except where the patient is proposed to be accommodated under Section 5 of the National Health Service Act, 1946 (which relates to accommodation for private patients).

(4) A medical recommendation for the purposes of an application for the admission of a patient under this part of this Act shall not be given by any of the following persons, that is to say (*a*) the applicant ; (*b*) a partner of the applicant or of a practitioner by whom another medical recommendation is given for the purposes of the same recommendation; (*c*) a person employed as an assistant by the applicant or by any such practitioner as aforesaid ; (*d*) a person who receives or has an interest in the receipt of any payments made on account of the maintenance of the patient ; or (*e*) except as provided by subsection (3) of this section, a practitioner on the staff of the hospital to which the patient is to be admitted.

Near relatives of the patient are also excluded from making such a recommendation.

Section 29

(1) In any case of urgent necessity, an application for admission for observation may be made in respect of a patient in accordance with the following provisions of this section, and any application so made is in this Act referred to as an emergency application.

(3) An emergency application shall be sufficient in the first instance if founded on one of the medical recommendations required by Section 25 of this Act, given, if practicable, by a practitioner who has previous acquaintance with the patient and otherwise complying with the requirements of Section 28 of this Act so far as applicable to a single recommendation, but shall cease to have effect on the expiration of a period of 72 hours from the time when the patient is admitted to hospital unless (*a*) the second medical recommendation required as aforesaid is given and received by the managers within that period ; and (*b*) that recommendation and the recommendation first referred to in this subsection together comply with all the requirements of the said Section 28 (other than the requirement as to the time or signature of the second recommendation).

(4) . . . Section 27 of this Act shall have effect as if . . . for " 14 days " there were substituted " three days."

Mental Health Review Tribunals

These bodies will be set up in each regional hospital board area to deal with applications. These will mostly be claims that a patient is not mentally disordered, or that, for various reasons, detention is unnecessary. The Minister may direct that a case be brought before a review tribunal. The tribunals will consist of one medical, one lay, and one legal member at least. Medical members are likely to have a long experience of psychiatry, and lay members will probably come from those with a record of public service, especially on hospital management committees. If satisfied with the evidence, the tribunal will have power to discharge patients from hospital.

Section 31 (4).—A patient . . . will apply to a Tribunal within a period of six months beginning with the day on which he is so admitted, . . .

Section 37 (1).—For the purpose of advising whether an application to a Mental Health Review Tribunal should be made . . . any medical practitioner authorized by or on behalf of the patient . . . may, at any reasonable time, visit the patient and examine him in private.

Any medical practitioner authorized under this section may inspect documents and medical records relating to the case.

Criminal Cases

If a person is convicted of a criminal offence and the court is satisfied on the evidence of two medical practitioners that the offender is suffering from mental disorder, the court may make a " hospital order " for admission for treatment. The doctor may have to give oral evidence, but there is provision for his report to be received without proof of signature. The effect of a hospital order is the same as that of an ordinary compulsory admission, but it cannot be terminated on application of a near relative.

Where it appears necessary for the protection of the public that discharge of the offender should be restricted, the court has power to do so. Discharge can then only be obtained by consent of the Home Secretary.

There is a curious provision in Section 36 of the Act which permits withholding of letters to and from the patient in certain circumstances. This applies if the medical officer thinks they might be harmful to the patient's progress or offensive to other people. The Minister, patient's Member of Parliament, and those having power over the patient are excluded from this potential censorship. Apart from ease of evasion, such interference with correspondence will be distasteful to most doctors. If a patient wants to write offensive letters, the recipient must make allowances for his mental state, and surely the risk to health from this cause could be dealt with informally.

It is only possible to give the provisions of the Act at the moment ; when it has been in operation for a year or two modifications will soon suggest themselves. It is a sign of enlightenment, and an important landmark in our treatment of mental illness. It is a full Act, but it is not unduly complicated.

MIDDLESEX HOSPITAL MEDICAL SCHOOL

The first phase of the Middlesex Hospital Medical School's rebuilding and development scheme was opened on December 16 by Lord ASTOR OF HEVER, the school's chairman, carrying out, as he said, a task which gave him greater pleasure and satisfaction than any other of a similar kind he has performed. No one more fitting could have been chosen to open the new building, since it was Lord Astor's gift of £400,000 which had made the building scheme possible, generously aided by Mr. EDWARD LEWIS and other benefactors, the University of London, and the University Grants Committee.

Sydney W. Newbery, London, S.W.

A large audience had assembled in the Edward Lewis Theatre, and Professor B. W. WINDEYER, the dean of the medical school, outlined the school's history and said that if the school were to maintain its standards and traditions more space was essential. The building scheme had therefore been divided into three stages, so that each could be used as it was completed. The present stage made available teaching laboratories and lecture theatres for the premedical and preclinical subjects of physics, chemistry,

(*Continued at foot of next page*)

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in common use.

Noscapine

"Coscopin" (Evans); "nicolane" (Aspro-Nicholas).

Pharmacology.—This is an alkaloid derived from crude opium, in which it constitutes 16–22%. The drug was formerly called narcotine. Since this name erroneously suggests that the drug is a narcotic, it has been replaced by the officially recognized name noscapine. It is more closely related to papaverine than to morphine or codeine. There is good pharmacological evidence, based on both animal and human experiments, that as a cough suppressant it has an activity comparable with that of codeine. It has no narcotic or analgesic effects. This is clearly advantageous in a drug required solely for suppressing cough though not necessarily in a sedative linctus to be given at night. The drug is free from the constipating effects of codeine, nor does it depress the respiratory centre. It does not produce addiction, and for this reason has been recommended by the World Health Organization expert committee on addiction-producing drugs as a substitute for codeine for suppression of cough.

Clinical Effects.—The chief therapeutic indication is for the control of excessive or unproductive cough. Limited clinical trials have shown that its effectiveness in controlling cough in a variety of diseases is similar to that of codeine and that the dose of 25 mg. for an adult is appropriate for this purpose. The absence of depression of the respiratory centre and of any sedative effects should make it superior to codeine when cough suppression alone is required. Toxicity is very low, and the drug can safely be tried in any condition in which a linctus is customarily given. A final verdict on its usefulness must await further clinical experience.

N.H.S. Basic Price.—Coscopin lozenges, 25 mg., 20 for 2s. 4d.; linctus, 25 mg. in 7 ml., 4 fl. oz. for 3s. Nicolane linctus, 15 mg. in 4 ml., 4 fl. oz. for 2s. 9d.

(*Continued from preceding page*)

and biology, physiology, pharmacology, biochemistry, and histology; student locker-rooms and lavatories, a reading-room, a staff dining-room, and a general purposes lecture-room; and lastly the medical school's pride and joy—the spacious Edward Lewis Theatre seating 391 people.

Lord Astor had met people, he confessed, though not many, who were indifferent to their surroundings—leaky roofs only added, as it were, to the brilliance of their work. Most people, he implied, would be more at home in the attractive surroundings of the new building which he had watched emerging from what seemed at first to be only an increasingly wide and deep hole. Great perception and sympathy were expected from doctors and surgeons. These qualities were not handed round on a plate, and he hoped that students might learn here in the new medical school how best to benefit and help mankind.

Dr. C. F. HARRIS, vice-chancellor of London University, spoke of the useful variety of the University's 12 medical schools, and said that the opening of the new school was a cause of rejoicing for all of them. Judging by the work produced in the old school the prospects for the new were dazzling.

Sir CHARLES DODDS, F.R.S., in a speech which revealed that he went surprisingly far back into the past, said that he had been at the Middlesex since 1916—just 80 years after the medical school was first opened, and he paid tribute to the dean's antipodean fervour, which had helped so materially to further this new stage in its history.

The afternoon's ceremony was a vivid illustration of Professor Windeyer's earlier remark that "the welfare and effectiveness of each—the hospital and the medical school—depend on the vitality of the other."

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

New Drugs for Depression

SIR,—We think it wise to draw attention to a potentially dangerous situation that is now arising with the introduction and widespread advertising of a whole range of new anti-depressant drugs. Very little has yet been published in Britain about the use of all these compounds, and the practitioner, who is starting to be bombarded with enthusiastic and often misleading literature put out by the various drug firms, may be unable to appreciate the very real risks he will often run in using them.

A paper from this department[1] recently described the value of iproniazid ("marsilid") in "atypical" depressive illnesses, a finding also confirmed by Alexander and Berkeley.[2] But iproniazid can sometimes be a toxic drug that causes severe liver damage. Only the fact that it seemed to help some long-standing and disabling depressive illnesses, unamenable to treatment by other methods, justified our continuing with it. Now several compounds have appeared, which it is hoped will be both non-hepatotoxic and anti-depressive in action, and we have been carrying out "blind" and other types of trial on these drugs, often using the patient as his own control.

Of the monoamine-oxidase inhibitors, isocarboxazid ("marplan") and phenelzine ("nardil") and probably phenylisopropyl hydrazide ("cavodil")—but we have used cavodil for only a few weeks—have a similar action to iproniazid and seem to be nearly as effective clinically. However, like iproniazid, they have certainly not, in our opinion, been able to replace electroconvulsive therapy in a large number of depressions, nor have they been found to be as effective in endogenous depressions as has often been claimed by the drug manufacturers; although they may sometimes have reduced the number of treatments required, and have prevented some of the relapses that can occur after an initial improvement with E.C.T. We have found their important use still lies in the treatment of reactive, anxious, and "hysterical" depressive states in good previous personalities in which the response to E.C.T. can often be so bad.

Nialamide ("niamid") seems to have quite a different action. It may even cause a marked and sometimes dangerous increase of anxiety in patients with certain types of depression. In fact, the only useful results seen with nialamide have been in patients with retarded depression and depressive hypochondriasis, and in this respect nialamide is more like imipramine ("tofranil") than the other monoamine-oxidase inhibitors. We have also not found imipramine to be very satisfactory in these neurotic depressions, which are better helped by amine-oxidase inhibitors, possibly because this group seems particularly sensitive to imipramine's side-effects. Fifty to sixty per cent. of patients with more typical types of endogenous depression have, however, been found to respond well to imipramine, provided one is prepared to wait long enough. But some of those who do not get better show, meanwhile, a greatly increased state of agitation and sometimes become serious suicidal risks. Undoubtedly many suicides are going to occur if general practitioners believe the drug manufacturers' claims that these drugs are as good as or can replace E.C.T., and if too many severely depressed patients are put on them and left untreated for too long with convulsive therapy.

As regards liver damage, several hundred patients have now been treated with phenelzine, isocarboxazid, nialamide,

and imipramine. No hepatic damage has yet been seen, as measured by serum glutamic oxaloacetic acid estimations and other liver-function tests. Two patients developed jaundice, one and two weeks after starting marplan and nardil respectively, but both had been on iproniazid for some weeks previously, and the jaundice was almost certainly due to that drug. Relatively few of our patients have had phenylisopropyl hydrazide cavodil, but in the U.S.A. there have already been reports of fatal jaundice and of colour blindness following its use, and we think that the doctors now being offered the use of this drug, after so very little testing in England, should be made aware of these risks, which are not mentioned in some of the advertising circulars being distributed.

It will probably be several years before the proper indications for the use of this interesting range of new drugs can be properly worked out, but the whole subject is full of fascinating promise. And we believe that some of the amine-oxidase inhibitors (*Journal*, December 5, p. 1238) will be found to be especially useful in the milder and more "atypical" depressions and fatigue states so often met with in general practice, and often never reaching psychiatrists. The drug companies are also naturally entitled to recompense for the valuable research work they have done on this new group of drugs, and the recent spate of advertising suggests that they are certainly out to get it. But it must not be at the expense of patients' lives. And this is certainly going to happen if some of these new drugs are not much more thoroughly tested in this country before being put on the market, and unless some of the present exaggerated advertising claims for them are modified and brought much more into line with current treatment reality.—We are, etc.,

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"Family Doctor" on Food

SIR,—I am reluctant to add to the embarrassment of *Family Doctor* following her recent matrimonial difficulties, but I cannot let pass without protest the December issue and accompanying booklet *All About Sugar*. The brightly coloured front cover of the magazine shows a child pouring sugar on to a bowl of refined carbohydrates which, supported by the contents of the booklet, constitutes a glaring advertisement for Mr. Cube.

The Editor of *Family Doctor* in his foreword to the booklet refers with obvious relish to small boys and girls who delight to "sink a spoon happily and splashily into a lovely mush of bread and milk and sugar." Other articles written by doctors give sugar a wonderful build-up as a food for health—especially desirable for the energetic child. Sugar-water is recommended for the restless babe who will not sleep, and glucose drinks (no brand mentioned) for hospital and convalescent patients. We are further told that the belief that sugar is bad for children's teeth just isn't true and that sugar has been accused quite wrongly of causing obesity. Apart from some reference to dental hygiene the whole contents of the booklet, supported by sugary pictures and syrupy recipes, must surely leave the lay reader in no doubt that doctors think sugar is a jolly good food which may be consumed in almost any quantity with impunity.

The most serious aspect of this matter is that it is so contrary to the health education policy of the British Dental Association as expressed in its recent *Memorandum on the Dental Health of Children*. This memorandum, drawn up by a panel of eminent dental surgeons, referring to the grave national scourge of dental caries, underlines the close association between caries incidence and the consumption of fermentable carbohydrates such as domestic sugar and glucose, noting also the absence of nutritionally protective factors in such commodities. Attention is further drawn to the marked improvements in the caries incidence during the first and second world wars when rations of sugar and sweets were greatly reduced.

One of the most difficult problems in current family nutritional education is to achieve moderation in the consumption of refined and stodgy carbohydrate foods, referred to in the latest *Annual Report* of the Chief Medical Officer of the Ministry of Health as one of the dangers of prosperous times; and which, as the dental *Memorandum* points out, "have the capacity not only to create a desire for more of the same type of food, but also take away the appetite for those other articles in the diet more necessary for body growth and health."

The British Medical Association appears prominently among the bodies listed by the British Dental Association who are urged to take note of and to further by any means in their power the spread of knowledge regarding the dental health principles specified in the *Memorandum*. That the popular health education journal of the B.M.A. should line up alongside the high-powered advertising campaigns for sugar, syrup, sweets, chocolates, confectionery, ice-cream, and iced lollies, against which the puny health educative resources of the local health authority are already powerless, is a deplorable state of affairs which prompts me to move for the withdrawal of *All about Sugar* from further circulation.—I am, etc.,

KENNETH O. A. VICKERY.

Health and Welfare Services Department,
County Borough of Eastbourne.

SIR,—In 1892 Sir James Crichton-Browne said, at a meeting of the British Dental Association, that the pulpy quality of the food described as bread deprived us to a large degree of the chemical element found in the husky parts of wheat. This was fluorine.

In the *Family Doctor* special pamphlet on bread (*Know and Enjoy Your Daily Bread*) I find a picture on page 3 which shows me that bread contains other things, but there is no reference to fluorine. Some years ago, in a letter to the *Journal* (1944, **1**, 708), I suggested that another valuable source of fluorine could be the finely divided stone dust from the Derbyshire gritstone or French burr-stone formerly used in flour milling. Both contain fluorine. This suggestion evoked no comment so I do not know if my idea was reasonable. But was Sir James wrong?

On pages 8 and 9 of the pamphlet I find a picture of the various forms of bread now obtainable. In the experience of most of us the larger the loaf the less crisp the crust; so why, if crust of any kind is good for the teeth, must we lose this as well as the useful friction action of the husk? Is it really true that it costs more to prepare bread, such as one sees in France, the French stick of the illustration? I doubt it.

In the experiment carried out in Duisburg (page 10) with underfed children one need not be surprised that the children grew well on any kind of bread. Surely

they ate other things as well? What the experiment does not show was the effect on the teeth, and I feel that the whole pamphlet carefully avoids any reference to the harm done to teeth by pulpy bread and also, as seems likely, by a shortage of fluorine. There would seem little point in experimenting with the addition of fluorine to drinking-water if it can be shown that a better bread, as advocated by Sir James so long ago, could correct the deficiency.—I am, etc.,

Hitchin, Herts. G. C. PETHER.

New Treatment for Chronic Bronchitis

SIR,—A letter signed by Professor J. W. Crofton and his team (*Journal*, December 5, p. 1251), attacking methods of publicity used for the promotion of the sale of a bronchitis remedy, clearly refers to "lomutherapy." This letter has revived my intention, after a delay of some months, to seek space in your columns for personal observations on this treatment.

The theory that finely powdered bronchodilators and enzymes should be effective and helpful in chronic bronchitis seems reasonable, and the papers by Robinson *et al.*[1 2] in October, 1958, suggested strongly that this approach to the problem held considerable promise. When Benger Laboratories announced in March of this year that this form of treatment was available, I determined to try it out in a group of bronchitics who have so far failed to respond, to any extent, to all other forms of treatment. I find that this group of patients acts as a most convenient yardstick by which to judge the efficacy of any new remedy, as any benefit produced in such cases would indicate that the new preparation is a true advance in treatment.

Treatment with "lomupren" and "lomudase" was commenced, and in a few days I had some most unpleasant experiences, as four patients became much worse and two had to be provided with domiciliary oxygen cylinders to tide them over until the ill-effects of the treatment had worn off. Both had had lomupren only. Three with lomupren and two with lomudase had definite toxic effects, mainly consisting of weakness in the legs occurring within an hour or two after having an inhalation. In my experience even 20 mg. of isoprenaline under the tongue has never cause this type of side-effect, while each powder capsule contained only 0.1 mg. of isoprenaline. As the nature of the diluent powder used in the capsule was not stated, I suspected that this might be the cause. Benger Laboratories disclosed that this is dextran powder, while reference to the original papers quoted freely in support of their claims disclosed that Robinson *et al.*[1 2] used lactose powder.

The response of the patients in this small trial was assessed clinically, according to subjective statements, and objectively by means of spirometry. A bronchodilator effect could be demonstrated shortly after using the powder, but some complained that it was irritating and caused them to cough. Marked subjective and objective relief was obtained in one allergic asthmatic, but this effect was lost after about ten days. His statement was proved true by spirometry, and it was then shown that an ordinary 1% isoprenaline spray had as good an effect as the powder had had initially.

These findings prompted investigation of the original papers by Robinson *et al.* on which this preparation is based, and it became evident that there is no evidence that the preparation used by them bore any clear relation to the Benger's product. Robinson *et al.*[1] used a mixture of the enzymes desoxyribonuclease and chymotrypsin, 5 mg. of each diluted with lactose powder. They did not mention how active these enzymes were and only give the quantity by weight. On the other hand, lomudase contains 0.01 "Anson units" of chymotrypsin alone, so that it is not possible to know what the comparative activity of these enzymes may be. One cannot compare the activity of one enzyme standardized for activity against two enzymes of unknown activity used together. Repeated perusal of the article by Robinson *et al.* reveals no evidence that these enzymes were used separately at any time, so that it is not possible to know which one produced the results. The second paper by Robinson *et al.*,[2] referring to the use of inhaled isoprenaline powder, fails to reveal exactly what dose of isoprenaline was used diluted in lactose powder, as they mention "Approximately 0.15 mg. of 1–5 μ, or 0.3–0.5 mg. of a 1–10 μ, isoprenaline powder (passed through a 300-mesh sieve) diluted with lactose." A little later, mention is made of the possibility of tolerance to isoprenaline developing in those patients "who inhaled 4.5 to 15 mg. of isoprenaline daily for up to eight months." Even if each capsule contained 0.5 mg., these people must have been using from 9 to 30 capsules a day—if they had been taking lomupren or lomudase 45 to 150 capsules. Figs. 2 and 4 in this paper refer to the response to the "optimal dose of isoprenaline powder," but it is not mentioned what the dose was or how it was arrived at. The Benger preparation, lomupren, on the other hand, contains 0.1 mg. isoprenaline sulphate *B.P.*, and lomudase the same dose in combination with the chymotrypsin.

The inhalation appliance for the Benger powder (issued by them) bears no similarity to that which was described by Robinson *et al.*, and in use is apt to become blocked. Furthermore, I have had complaints from a local chemist that the capsules tend to become damp in stock.

The use of dextran as a diluent may cause development of allergy towards it, and I can find no trace of any work where dextran powder has been tried out either in man or animals to find out if it has any toxic effect or not. It seems incorrect that *all* the contents of the powder capsules should not be declared on the container, and it seems quite wrong to have thousands of people inhaling dextran when nobody knows what its long-term effects may be. We are all conscious of the effects of inhalation of many other industrial dusts, and I consider that the condition of the advanced bronchitic is bad enough without running the risk of any further deterioration from dextran inhalation. The only explanation for the weakness of the legs which occurred in five patients seems to be the dextran powder, as it and the isoprenaline are the only common factors between the two preparations, and isoprenaline could not have caused this effect in such a small dose.

"Lomutherapy" has been used by me in sixteen patients, and in no instance has it been shown to be more effective than an isoprenaline spray. In five cases there were toxic effects mentioned before, and definite worsening in four. I was conscious that the group of bronchitics might have been too severe to have been helped by any form of therapy, therefore seven cases of medium severity were included. These cases did not have toxic effects, but no advantage over isoprenaline could be demonstrated. One further bronchitic who became worse and had to be admitted to hospital has been encountered recently where lomudase had been given by the general practitioner. During the week he received this treatment his clinical condition steadily worsened and his doctor spontaneously suggested that the lomudase might have been responsible.

In view of my experiences I did not feel it justifiable to use this preparation any more, as I did not think it would be fair to the patients, and I communicated my views to the Benger Laboratories representatives. My analysis of the publications on which "lomutherapy" is based suggests that the good effects reported could have been due to the desoxyribonuclease, as reported by Salomon *et al.*[3] Benger Laboratories appeared to be so convinced that their preparation had already been proved by the work carried out by Robinson *et al.*[1 2] that no samples for clinical trial were available. I feel strongly that it is not correct to try out new preparations

at the expense of the National Health Service, but I was forced to prescribe these appliances before I found out that the preparation was no more useful than an isoprenaline 1% spray.—I am, etc.,

Derby Chest Clinic. H. MORROW BROWN.

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1. Robinson, W., Woolley, P. B., and Altounyan, R. E. C., *Lancet*, 1958, **2**, 819.
2. —— Ibid., 1958, **2**, 821.
3. Salomon, A., Herchfus, J. A., and Segal, M. S., *Ann. Allergy*, 1954, **12**, 71.

SIR,—The welcome letter and leading article in your issue of December 5 (pp. 1240 and 1251) rightly emphasize the singularly unconvincing evidence for the efficacy of "lomudase" and "lomupren." A recent article[1] based entirely on the subjective effects of these substances is equally lacking in reliability when trying to assess them. The method of sputum viscosity measurements employed by Robinson *et al.*[2] when investigating the effects of inhaling desoxyribonuclease and chymotrypsin are crude when compared with previously described methods.[3 4]

We have as yet no objective support for the assertion that the particles of either lomupren or lomudase reach the lower bronchi or bronchioles, where both spasm and accumulation of thick sputum are maximal. Another drawback of this treatment is the loss of efficiency of the "lomulizer" in emphysematous patients who have gross diminution of inspiratory power, which is by no means overcome by the use of the hand-bulb.

Apart from the question of publicity, with which I am in full agreement with you, Sir, and with Professor J. W. Crofton and his colleagues, we have still much to learn about the reduction of the viscosity of sputum in chronic bronchitis.—I am, etc.,

London, N.W.2. D. S. NACHSHEN.

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1. Carnachan, G. A., and Bendall, A., *Brit. J. clin. Pract.*, 1959, **13**, 703.
2. Robinson, W., Woolley, P. B., and Altounyan, R. E. C., *Lancet*, 1958, **2**, 819.
3. Blanshard, G., *Arch. Middx Hosp.*, 1955, **5**, 222.
4. Elmes, P. C., and White, J. C., *Proceedings of Second International Congress of Rheology, Oxford*, 1953, p. 382.

SIR,—I feel that a reply to the letter (*Journal*, December 5, p. 1251) by Professor J. W. Crofton and his colleagues is very necessary, especially in view of the discrepancy between his and my results with the "lomu" products. Professor Crofton, on his own admission, has treated several patients for obviously only a few weeks. I, however, have treated 35 patients, 16 for three months and over. I am hoping to publish at the end of this winter the results of a general-practitioner trial on the use of "lomupren" and "lomudase." However, the following is, by necessity, a very brief and incomplete résumé of my experiences with the "lomulizer."

My practice is in an industrial area of London which has a heavy dust-laden atmosphere. All the patients, prior to this treatment, had a long history of chronic bronchitis and/or asthma. In many cases they have been in hospital several times a year, and have been on continuous antispasmodic therapy for many years. An overall impression of the results so far has been one of astonishing success. Of the 35 cases, two have been complete failures, and the rest have shown very noticeable improvement, especially in the following four cases:

Case A.—Male, aged 40. In the last two years has been to work for a total of eight weeks. Has a long history of hospitalization. Since lomu therapy, has been to work continuously for four months at his original job, involving indoor and outdoor work.

Case B.—Male, aged 58. When first seen four months ago was thinking of retiring from his work (dustman) owing to recurrent attacks of chronic bronchitis. Rarely at work for longer than two weeks at a time. Since lomu therapy commenced has been back at work, and lost only one week owing to bronchitis.

Case C.—Male, aged 34. Recurrent attacks of status asthmaticus for years: treatment at the Brompton Hospital and the Central Middlesex Hospital. Had been told that nothing further could be done for him. Seen in status asthmaticus of 16 hours' duration. Over the course of 36 hours was given aminophylline, 54 min. (3.2 ml.) of adrenaline, 5 gr. (0.32 g.) ephedrine, aminophylline suppositories, sedation, etc. After one lomudase cartridge, sputum was liquefied and expectorated, and the asthmatic attack subsided.

Case D.—Female, aged 56. An unsolicited testimonial was afforded by the following paragraph in a letter concerning the examination of one of my patients by a chest physician. "At the commencement of the examination there were scattered rhonchi throughout the lungs, but these responded rapidly to an atomizer she had with her." The atomizer was the lomulizer.

Could it be that Professor Crofton and his colleagues failed either to continue therapy for long enough, or, more important, take sufficient time and trouble to explain the way to use the atomizer in a proper manner? I conclude with the hope that no general practitioner will be dissuaded from trying this new product by the remarkably incomplete investigations of Professor Crofton and his colleagues.—I am, etc.,

London, N.W.10. D. TILLEY.

Antibiotic Therapy in Chronic Bronchitis

SIR,—Two elderly chronic bronchitics are facing the prospect of another English winter. One is a man aged 63, still at work. The other is a woman aged 66, no longer working. In all other respects their cases are identical. Both are on continuous antibiotic cover, which costs the nation approximately £60 for six months' treatment (*Journal*, December 12, p. 1315). The patients derive equal benefit from treatment. In the case of the man, the cost of treatment is offset by the extra number of man-hours he is able to put in at work during the winter months. In the case of the woman, there is no corresponding financial advantage. Who is to tell me that I should withdraw treatment from the woman, and not the man? And when the man retires at 65, should I refuse him treatment the following winter?—I am, etc.,

Yaxley, Peterborough. CYRIL HART.

Recording Speech and Respiration

SIR,—Mr. L. R. C. Haward's statement (*Journal*, November 28, p. 1178) that I had found a throat microphone to be sensitive enough to permit respiratory sounds to be measured during playback rests on a misunderstanding, and I am not surprised that he had difficulties with this method of recording respiration. I used the throat microphone for obtaining a visual voice record while respiration is recorded through the usual microphone on to sound tape. The paper to which Mr. Haward refers[1] distinguishes between voice tracings obtained from the throat microphone which feeds speech *movements* into the polygraph, and "*inspirations* which were clearly audible on good-quality recordings." In connexion with the latter it gives reference to my

original paper on speech-breathing activity,[2] containing the detailed description of the method of recording breath rate during speech. By this technique the respiration rate and the "output per breath" (i.e., the number of syllables per expiration) can be measured. These measures have proved highly significant indicators of emotional states, as I was able to show.[3]

The value of my method of measuring breathing during speech is that it does away with the necessity of using restrictive devices which alter the nature of breathing patterns. The patient is unencumbered by any additional apparatus and unaware of his breathing being recorded.—I am, etc.,

Department of Phonetics,
University College London. F. GOLDMAN-EISLER.

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[1] Goldman-Eisler, F., *J. ment. Sci.*, 1956, **102**, 78.
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[3] —— *Brit. J. med. Psychol.*, 1956, **29**, 35.

New Sulphonamides

SIR,—We have read with great interest your leading article entitled "New Sulphonamides" (*Journal*, September 19, p. 482). We were specially interested in sulphamethoxypyridazine, which is reported to possess a number of excellent properties—viz., prolonged action, good absorption, slow excretion, poor acetylation in blood, good antibacterial activity, etc.—which suggest it may be a very valuable drug.

Sulphamethoxypyridazine, being a long-acting sulphonamide, might be expected to be more effective in plague than other known sulphonamides like sulphadiazine. We therefore carried out a trial of sulphamethoxypyridazine in experimental plague in mice, using sulphadiazine as a control. Our results[1] showed that sulphamethoxypyridazine had no greater curative effect than sulphadiazine. Indeed, in that the latter drug is reported to have the lower oral toxicity, sulphadiazine could be said to be superior.

Our findings in experimental plague show that inferences based on studies of drug concentrations in body fluids, drug clearances, etc., may sometimes be misleading.—We are, etc.,

AMINA BUNDEALI.
M. K. HABBU.
C. V. DELIWALA.
Haffkine Institute,
Bombay, 12, India.

REFERENCE
[1] Bundeali, A., Habbu, M. K., and Deliwala, C. V., *Indian J. med. Sci.*, 1959, **13**, 423.

Griseofulvin

SIR,—I have read with interest the careful appraisal of griseofulvin in the treatment of fungous diseases of the skin by Drs. Martin Beare and Donald Mackenzie, and by Dr. A. J. E. Barlow and his co-workers (*Journal*, November 28, pp. 1137 and 1141). Our preliminary observations[1] and follow-up closely parallel those of Drs. Beare and Mackenzie in tinea capitis. Although the majority of our cases were caused by *Microsporum audouini*, we have also in several cases observed the persistence of viable spores in debris and hairs after the disappearance of fluorescence. Hairs from one particular case gave repeated positive cultures up to three months after becoming Wood's-light negative. Like Drs. Beare and Mackenzie, we used no local application during griseofulvin therapy, but we now feel that frequent shampooing and the topical use of antifungal remedies may hasten the rate of cure. Although we have treated fewer cases of *Trichophyton tonsurans* infection, we have come to the tentative conclusion that they clear up more quickly, judging from persistent negative cultures after three to four weeks' treatment. There seems to be little doubt that cases of tinea capitis require to be closely supervised for long periods. Our minimal requirements to judge a child free from infection are three negative cultures at monthly intervals after the disappearance of fluorescence or clinical cure. At present it is hard to know at what stage griseofulvin can be stopped safely.

Our experiences in two cases of tinea barbae (*Trichophyton verrucosum*) were similar to those of Dr. Barlow and his colleagues. Both patients experienced subjective improvement, judging by diminution of itching and burning, after a week's course of griseofulvin, but it was not considered that the rate of cure was significantly altered. Results in two cases of kerion were not very encouraging.

The question of toxicity must still be regarded as *sub judice*. In our first 12 cases, bone-marrow activity and liver and renal functions were closely studied. No deviation from normal patterns was found. However, since then a sharp drop in the relative polymorph count has been observed in four children during treatment. The polymorphs recovered their normal values when the drug was stopped and the children apparently suffered no ill effects. It is now our routine practice to do total white cell and differential counts at two-week intervals during treatment. While all these little local difficulties must be borne in mind, there is no doubt, as you say, Sir (*Journal*, November 28, p. 1165), griseofulvin marks a revolutionary advance in the oral treatment of ringworm infections.—I am, etc.,

F. O. C. MEENAN.
St. Anne's Hospital,
Dublin.

REFERENCE
[1] Meenan, F. O. C., and O'Connell, L. G., *Irish J. med. Sci.*, 1959, **6s**, 360

Imipramine in Depression

SIR,—I read with interest the paper by Drs. J. R. B. Ball and L. G. Kiloh (*Journal*, November 21, p. 1052) on controlled trial of imipramine in treatment of depressive states. I am acquainted with the papers mentioned by Drs. Ball and Kiloh, and I have treated 65 cases of endogenous depression, most of them coming within the category of agitated depression. In general I would concur with what Drs. Ball and Kiloh have to say. I must, however, make one reservation, and that is the reason for this letter.

As stated above, most of my cases were suffering from agitated depression, the depression varying in intensity. At first all the cases treated were started on imipramine, but it was soon evident that they could not tolerate imipramine on account of increased anxiety, restlessness, or agitation. A different method was then adopted. The patient was advised to take either chlorpromazine or trifluoperazine for a few days, and then imipramine was added. Imipramine combined with one of the phenothiazines has been used by Delay and Deniker,[1] and they also found this combination gave better results than with imipramine alone.

As to the indications for imipramine, I fully agree with Drs. Ball and Kiloh that by using this drug, and, in my series, by using it in combination with trifluorperazine or chlorpromazine, the patients could continue with their work or could return to their work much sooner than with the previous forms of treatment. Imipramine does not replace electroconvulsive therapy (E.C.T.) because, as was agreed at the symposium in Cambridge, in the more serious forms of depression there is no response to

imipramine. The risk of suicide being very great, it would be dangerous to start treatment with imipramine alone without prior E.C.T.

To illustrate my findings, here are the details of a case of a woman aged 47 with recurrent depressive episodes with agitation. She spent 12 months in hospital, receiving three series of E.C.T., and after each series she was better, but she did not maintain her improvement. In February of this year she was put on imipramine. She could not tolerate imipramine well at first, on account of increased feelings of agitation and distress. Trifluoperazine was then added, and the patient soon felt more at ease and there was a steady improvement in the level of her mood. She was discharged from hospital eight weeks after starting on this combined treatment and could resume her normal occupation, which is one of teaching, almost immediately. She is continuing with her work, but she must, however, take up to 150 mg. of imipramine a day and 5 to 7 mg. of trifluoperazine daily. Whenever she tries to discontinue the trifluoperazine her agitation increases. Equally, when she gradually reduced the imipramine to 75 or 50 mg. daily, her depression deepened.

Because of this, and of the accepted side-effects, when treating patients with imipramine for an agitated depressive condition, I think that the combined treatment must be thought of first.—I am, etc.,

Mabledon Hospital, Dartford, Kent. G. Bram.

Reference

[1] Delay, J., and Deniker, P., *Canad. Psychiat. Ass. J.*, vol. 4, special supplement, 1959.

Family Planning Advertisement

Sir,—I understand that the decision of Council not to accept the Family Planning Association's advertisements was based on the false idea of maintaining unity in the membership at this crucial moment when the Royal Commission on Doctors' and Dentists' Remuneration is about to report. I cannot imagine a more fallacious argument for a sacrifice of principle. Could anything be more damaging to the reputation of Council than a charge of "moral cowardice"? What trust can the profession have in its leaders to deal with the Government when they behave in this manner towards a minority section of opinion in their own ranks? It is to be hoped that the Council will reconsider its decision in the light of the following:

1.—In 1958 the Lambeth Conference passed the following resolution: "The Conference believes that the responsibility for deciding upon the number and frequency of children has been laid by God upon the consciences of parents everywhere: that this planning in such ways as are mutually acceptable to husband and wife in Christian conscience is a right and important factor in Christian family life, and should be the result of positive choice before God. Such responsible parenthood, built on obedience to all the duties of marriage, requires a wise stewardship of the resources and abilities of the family as well as a thoughtful consideration of the varying population needs and problems of society and the claims of future generations." Thus speaks the considered voice of the bishops of the Church of England.

2.—The Royal Commission on Population reported as follows in 1949: "The most significant feature of this adjustment [to modern conditions], in our view, is the gradual acceptance of control over the size of one's family by means of contraception as a normal part of personal responsibility . . . no changes in the social environment are likely to lead men and women to abandon this means of control over their circumstances." And again: "The giving of advice on contraception to married persons who want it should be accepted as a duty of the National Health Service, and the existing restrictions on the giving of such advice by public authority clinics should be removed. The initial duty to give advice should rest with the family doctor."

3.—In the debate in the House of Lords in July, 1959, on the advisability or otherwise of permitting the Bishop of Southwark's appeal on behalf of the Family Planning Association over the B.B.C. network on August 23, the Archbishop of Canterbury said that: "The Roman Catholic Church is taking part in the work of family planning throughout the world, and all other churches are only too glad to co-operate with them and respect their own traditions wherever possible. It ought to be made quite clear that the Roman Catholic Church is as deeply involved in family planning as any of us." In the same debate Lord Chesham, for the Government, said: "If this is to offend a certain weight of opinion in this country, and if we are to be accused of committing a political 'gaffe' in allowing the broadcast, just think of the colossal weight of opinion which is going to be offended if we do not."

4.—Again *The Times* of December 12 says in a leader: "A healthy tradition of British public life allows the fullest reasonable freedom of speech and action to minority pressure groups. But the line should be drawn against allowing them to have their way to the extent of coercing the majority. Such coercion seems to have been successfully applied to the British Medical Association."

I would add that Council's action is an insult to the memory of Lord Horder, who was the late president of the Family Planning Association, and to Sir Russell Brain, who is its present president. What is even worse is the face that Council presents to the public. In 1959 they behave still in the way they behaved in the last century, when they refused to admit women doctors to membership. As this is now nearly 1960, I hope Council will think again.—I am, etc.,

London, W.C.1. J. L. McCallum.

Sir,—I see in *The Times* of December 10 that the Council of the B.M.A. have, as a result of protests from Roman Catholic doctors, withdrawn a two-page advertisement for the Family Planning Association. I write to draw the attention of members of the B.M.A. who may not take *The Times*, or who may not have noticed the paragraph, to the actions which are being taken in their name by the Council of the B.M.A.

I think that most non-Roman-Catholic members consider that the Family Planning Association is doing a good job and should be helped in every way possible. The advertisement would have spread knowledge of the Family Planning Association to many readers, and it does not appear to me to be in keeping with a liberal profession to prevent the spread of knowledge. I consider, and I think it is a majority view, that the public, our patients, are deprived of such knowledge to their detriment.

It is time we woke up to what is happening as a result of minority pressure groups, and I would urge every member who thinks as I do, to write asking the Council of the B.M.A. to reverse their decision on this matter. I would also urge that the matter be brought before Divisional Executive Committees and protests from all sides reach the ears of the Council.—I am, etc.,

Risca, Mon. M. T. Wade.

Breast or Bottle?

Sir,—Your leading article (*Journal*, December 5, p. 1239) should provide some new facts for discussion and cause us to consider whether we should allow breast feeding to become extinct in favour of synthetic feeding. The assertion that the incidence of infection was the same in the British series whether the babies were breast-fed or artificially fed, and only slightly increased in artificially fed infants in the Swedish series,

requires the qualifying statement that this was so only as far as the observations were carried—perhaps one year. To test the true resistance of the two groups of infants it would be necessary to record the infection rate when they left the sheltered home environment and entered the arenas of school life at 5 or 6 years old until the age of 7.

It is difficult to explain the lack of correlation between the British and Swedish authors' figures for the physical development of infants on different feeding regimes. From a practical point of view it is common for infants on full-cream dried milk to make astonishing weekly gains of half to one pound (0.27–0.45 kg.) a week, and to pass the six- and twelve-month milestones many pounds ahead of the standard tables. As a rule, breast-fed babies gain a modest four to six ounces (0.11–0.17 kg.) weekly. All full-cream dried-milk powders, when reconstituted by dissolving one part in eight of water, become cow's milk containing nearly three times as much protein as does breast milk. This is good for the calf, which grows four times as fast as a human baby. But should we not consider the effect of this large daily dose of foreign protein on the infant's metabolism? This substance stimulates the latter 20% as compared with the stimulus of about 4% to 6% provided by fat and carbohydrate. Physical growth is grossly disturbed by such a stimulus, and one may speculate with the Swedish authors as to whether there are occult disadvantages being laid down in the developing human personality created by the strain of excessive physical development.

There is no certain evidence presented in your review of these surveys to confirm the superiority of synthetic feeding. Human lactation is the successful result of probably a billion years of evolutionary experiment. Modern science has tried artificial feeding as an approved general policy for less than a century. It will probably take another million years to learn the answer to the question "Breast or Bottle?"—I am, etc.,

Romford, Essex. P. D. MULKERN.

H3 Developments

SIR,—I have read the annotation under the heading "H3 Developments" (*Journal*, December 12, p. 1317). My name is referred to as one of an advisory panel of doctors given in their publicity material.

I am in no way connected with this organization; and as long ago as last October, when the use of my name in this connexion came to my notice, I immediately wrote H3 Developments a letter of protest, a copy of which I also sent to the Secretary of the B.M.A.—I am, etc.,

London, S.W.3. T. MARKOWICZ.

Retinal Burns After Sun's Eclipse

SIR,—The production of retinal burns from looking at the sun is a fully recognized and well-annotated occurrence (Duke-Elder[1]). It is therefore all the more regrettable that the recent partial eclipse of the sun on October 2, which attracted an unusual amount of attention in the national press, should have had the unfortunate consequences here reported.

In this area, with an approximate population of 500,000, at least 15 cases of this condition, occurring mainly in children, have been seen, and, in the majority, permanent retinal damage and partial loss of central vision have resulted. Fortunately most appear to have used only one eye to look at the sun. A number were aware of the danger and used negatives or tinted glasses without being aware of the relative inefficiency of these filters. The unilaterality of these cases is apparently in contradistinction to the findings reported by Duke-Elder.

If this area is representative, these findings suggest that, totally unnecessarily, at least 500 eyes have been permanently damaged over the country as a whole. Should not this be a stimulant to the very widest efforts at proper education of the public before the stars in their courses bring about the next solar obscuration? A notable feature of the present series was the apparent ignorance of the presumably educated and intelligent adult (headmaster, parent, etc.) of the danger of looking directly at any strong source of light.—We are, etc.,

M. J. GILKES.
D. G. MACPHERSON.
A. H. OSMOND.
B. THORNE THORNE.
D. ST. CLAIR ROBERTS.

Sussex Eye Hospital, Brighton.

REFERENCE

[1] Duke-Elder, Sir Stewart, *Text-book of Ophthalmology*, 1954, Vol. 6, p. 6,494. Henry Kimpton.

Why Patients Go To Hospital

SIR,—In the course of his interesting article (*Journal*, December 12, p. 1322) Dr. John Fry asks whether the hospital is providing adequate facilities for its local doctors. One of the conclusions that he draws from his own statistical records is that the least satisfactory results of hospital treatment were (amongst others) in patients suffering from rheumatic disorders. He makes no mention in his tables of having referred those patients to a special rheumatological department, so we may presume that there is not one available in his area. Surely this fact, if true, partially answers his initial question; for according to his figures the need is great.—I am, etc.,

The West London Hospital Medical School, London, W.6. W. S. C. COPEMAN.

Reading the Number Plate

SIR,—I have been consulted on a number of occasions by applicants for driving licences who have been rejected owing to their alleged inability to read a number plate at 25 yards (30 m.). On examination, quite a considerable proportion of these were found to satisfy this requirement without any difficulty. On inquiry, I was informed that at the time of the test the number plate was not readily legible owing to poor lighting conditions, or in the opinion of the applicant the distance was in excess of 25 yards.

That the test in this respect is unreliable is quite apparent and is open to considerable criticism. An examination of number plates will readily reveal how unreliable the present haphazard test is. Number plates vary very considerably in legibility. There are white enamel letters on black backgrounds, aluminium letters of varying degrees of brightness and clarity on black or grey-black backgrounds, frequently soiled with varying amounts of mud or grime. The number plate may have the sun shining directly on it, or it may be more or less shadowed. All these, and no doubt other factors, tend to make for inconsistency and uncertainty.

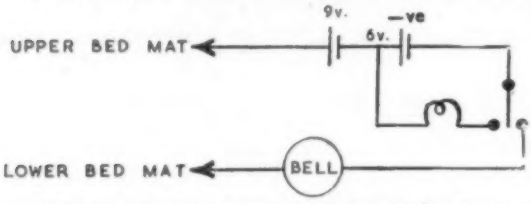
The varying degrees of contrast between the number and the background can and do affect the legibility very considerably.

I suggest that some uniformity be achieved in carrying out this test, which should be conducted in controlled conditions, and that a certificate from an approved ophthalmic examiner be accepted without question, or possibly even be required.—I am, etc.,

London, N.21. S. CHAPLIN.

"Do-it-Yourself" Enuresis Alarm

SIR,—I was so appalled by the price of the enuresis alarms mentioned in one of the articles you printed some months ago that I resolved to make one myself and to see what it would cost. The circuit is shown in



the Figure, and a list of the parts with their *retail* prices is appended below:

	s.	d.
Bell	7	8
Two-way switch	3	0
Bulb holder		6
Bulb		10
Two battery clips		8
Three battery terminals	1	0
Wire	1	0
Grid-bias battery	2	9
Wooden box		
	17	5
Two pieces of monel metal gauze, 24 by 18 in. (61 by 46 cm.) ...	17	6
Waterproof adhesive plaster for binding	3	0

The assembling took two hours, but it could no doubt be done much more quickly with practice. It remains only to say that my machine works satisfactorily, and to ask why a commercial machine should cost upwards of six guineas.—I am etc.,

Madeley, Shropshire. J. B. METCALFE.

Organic Aetiology in Psychiatry

SIR,—From Dr. Philip Hopkins's letter (*Journal*, November 21, p. 1098) it would seem that even psychiatrists are not free from the influence of Virchow, and must explain all disease in terms of morbid anatomy. The teaching that all lesions must be either congenital, traumatic, inflammatory, or neoplastic dies hard. Whereas it soon becomes apparent in general practice that a large number of patients present with symptoms of disordered emotion rather than of morbid anatomy. Fear, guilt, anxiety, anger, are all potent agents in producing psychosomatic illness as well as in modifying organic disease processes.

Some of these emotions, like fear of cancer, or fear of pregnancy or of losing one's job, are obvious and usually respond to simple measures like adequate explanation and reassurance. But others have been repressed and need ferreting out, and it is here that the practitioner who knows the family background is often so well fitted to help. Most of us have had to learn these truths the hard way and are only now, after many years of practice, beginning to realize their full significance. One of the best ways to help younger colleagues to appreciate these problems is surely for them to come as students and live for a while in general practice; or, after qualifying, for them to do a trainee assistantship with a principal who has both the time and inclination to discuss these patients.—I am, etc.,

Blandford, Dorset. CHARLES E. LANGLEY.

Human Growth

SIR,—May I avail myself of the courtesy of your columns to correct some wrong impressions which your reporting of my paper at the Symposium on Human Growth (*Journal*, December 5, p. 1248) might convey? There are three points in particular to which I refer.

1. "Increase in children's size over the period 1931–41 was different in different age groups." The point made was that 5-year-old children born in 1931 were taller than those born in 1921 by about the same amount as those born in 1921 were taller than children born in 1911, but that 5-year-old children born in 1941 were little, if any, taller than the 1931 group of children. On the other hand, 8-year-old and 12-year-old children appeared to have increased in height by about the same amount between these decades.

2. "For a given age between 1948 and 1953 boys were increasing their advantage over girls in height and catching them in weight." This statement refers to samples of 14-year-old children, an age when the adolescent growth spurt is strong in boys and is almost complete in girls.

3. "In Aberdeen the I.Q. at age 11 was decreasing in boys but increasing in girls." The point made was that there was evidence from the literature that the intelligence of girls in this country as measured by the results of the 11+ Moray House Test had been increasing relative to that of boys between 1932 and 1947, and that from the results of Aberdeen children sampled in 1947, 1951, and 1957 this trend appeared to be continuing.

I am aware of the impossibility in the space at your disposal of reporting fully on such a symposium, and would like to state for the benefit of interested readers that the Society for the Study of Human Biology will publish the papers in full at some date in the near future.—I am, etc.,

Bucksburn, Aberdeen. A. W. BOYNE.

Beyond a Joke?

SIR,—I never thought that you would allow advertisements to appear in the *Journal* like some of the advertisements one sees on a television in this country, the latest example being the one that appeared in the *B.M.J.* of December 12 (p. 37 of the advertisements) by a shipping firm. It beats the lot. In this advertisement two pictures of Mr. B. S. appear. Fig. 1 "Mr. B. S. before his trip (? with bands)," a bulging, drooping figure; and Fig. 2 "Mr. B. S. on return (? without)," a virile and muscular figure. Mr. B. S. is supposed to have made £150,000 through a successful business deal.

The *B.M.J.* is read mostly by the members of the medical profession. You must have a pretty poor opinion of the medical profession to swallow that advertisement. So I say, come off it: the income from the advertisement may be good, but it is in bad taste. It stinks.—I am, etc.,

Liverpool, 18. H. J. PRATAP.

Volume 104

SIR,—I should be grateful to know why the volume numbers of your excellent journal perpetually oscillate between 1 and 2. Since my work has taken me into the field of medical literature I have realized that this convention is a constant source of perplexity to overseas medical writers, and is more than a minor cause of irritation to printers, editors, and others who face the hazards of transforming manuscript into print.

I suggest, Sir, that your first issue of the forthcoming year should carry the unequivocal volume number **104**. No one nowadays believes that the *B.M.J.* is in its infancy, and to reveal that in fact it is a centenarian would cause neither surprise nor concern. I am sure that the characteristic vitality of your publication would prove that venerable old age and senility do not, by any means, go hand-in-hand.—I am, etc.,

ANTONY DUGGAN.

The Wellcome Museum of Medical Science,
London, N.W.1.

POINTS FROM LETTERS

National Society of Non-Smokers

The Rev. HUBERT V. LITTLE (Secretary, National Society of Non-Smokers, 138, East Dulwich Grove, London, S.E.22) writes: The public-spirited lead given by Messrs. Marks and Spencer's, in inaugurating last week a "No Smoking" régime in all their 237 stores throughout the country, is one which, one hopes, will be followed by many other—especially food—establishments. Our Society is pressing for this, and would be grateful to hear from readers who support our campaign.

An Accident Service for the Nation

Dr. S. LANCASTER (Caerwys, Flints) writes: The Japanese Red Cross Society's Report (1957) on the "Atomic and H Bombs" describes the result of the bomb on Hiroshima. The Red Cross Hospital was not damaged but was overwhelmed with casualties, queues stretching along the streets for long distances. The doctors and nurses of Hiroshima were mainly casualties themselves. . . . As a casualty officer I know that a sudden influx of accident cases taxes the casualty staff. In case of a hydrogen bomb explosion the staff, if alive, could not cope with much more than the usual number of casualties.

Parental Age and Cancer

Dr. R. TUDOR-EDWARDS (Stanmore) writes: It has struck me for some years that children whose parents live to a very old age are more liable to develop cancer than those whose parents live the normal span of life. I saw my first case of cancer of the lung 37 years ago in a woman who died at 34 years of age. She was an only child, but her father died at 84 years of age and her mother at 103 years of age. The oldest parent in my practice died at 105 years of age, but a child developed cancer at 38 years. Two parents still alive aged 90 and 88 years had a child who developed cancer at 38 years; similarly two parents aged 91 and 92 years had a child who developed cancer at 40. . . . I wonder whether any of my colleagues may have noticed this.

Lung Cancer in White South Africans

Dr. LETITIA S. MCINTYRE (Stirling) writes: In his conclusions in an article on "Lung Cancer Among White South Africans" (*Journal*, October 31, p. 852) Dr. Geoffrey Dean states that the same type of tobacco formed the basis of cigarettes in both the U.S.A. and the U.K. In fact there appear to be certain differences, notably the fact that "stem" is incorporated in the tobacco used in the manufacture of the average cigarette sold in the U.K. This practice has obtained since the last war at any rate. "Stem" is not incorporated in the average U.S. cigarette.

Obituary

J. H. ALLAN, M.R.C.S., L.R.C.P.

Dr. J. H. Allan, who was a general practitioner in Chorley, Lancashire, for forty years, died on October 27, 1959, at the age of 73.

John Harrison Allan was the eldest son of the late Dr. and Mrs. James Henry Allan, of Liverpool, and brother of the late Captain Noel James Allan, M.B., R.A.M.C., and of the late Dr. James Shewen Allan, medical officer of health of Chester-le-Street. He studied medicine at Liverpool University, qualifying in 1919. For a period after he had completed his resident appointments he assisted the professor of midwifery at Liverpool both in teaching at the university and in the clinical work of the Maternity Hospital. It naturally followed that when he joined the late Dr. Lea in partnership in Chorley soon afterwards much of this time and skill were devoted to midwifery. At the Chorley Cottage Hospital he did most of the operative surgery required by his patients up to the time the N.H.S. was introduced, and he was always specially interested in the ophthalmic side of his practice.

Among the professional appointments he held were those of certifying factory surgeon and treasury medical officer for the area. He was assiduous in carrying out his duties on various medical committees and was the profession's local representative on the Lancashire medical committee and on the management committee of the Preston and Chorley hospitals. During the second world war he held the rank of major in the 12th Lancashire battalion of the Home Guard.

Nature had liberally endowed Dr. Allan with a fine intellect, handsome appearance, and much charm of manner, to which was added a keen sense of humour. His unbounded energy and interest in his work were reflected in the extensive general practice in which he was engaged up to the time of his death. Our deep sympathy is extended to his widow, two sons, and five daughters.—F. J. D.

E. E. MATHER, B.M., B.Ch.

Dr. E. E. Mather, who formerly practised in Liverpool, died in that city on November 3, 1959, at the age of 71.

Edward Elton Mather was born at Lydiate, Liverpool, in 1888, and was educated at Malvern College, Exeter College, Oxford, and St. Bartholomew's Hospital, where he qualified in 1913, graduating B.M., B.Ch. in the following year. Shortly after the outbreak of the first world war he joined the R.A.M.C. During the German offensive of March, 1918, he was taken prisoner, being unable, owing to the rapidity of the enemy's advance, to evacuate his forward dressing-station in time to avoid capture. In captivity he suffered such severe privations and ill-treatment that he was practically an invalid when repatriated after the armistice. After convalescence he took up a post as medical officer at Cadbury's Bournville works, but he finally settled in general practice in Liverpool in 1927.

During the second world war he did not escape the overwork general to medical practitioners of his generation, due to the absence on active service of their younger colleagues. This undoubtedly contributed to a breakdown in health at the end of the war which necessitated a somewhat premature retirement from practice. During the war he had been active in examinations of recruits to the Forces on behalf of the Ministries concerned, and after his retirement from general practice he was able to maintain this contact with medical work until he died.

His main interests outside his profession centred on the study of modern languages and natural history. He leaves a widow, two sons, and a daughter.

H. H. DUNLOP, M.B., Ch.B.

Dr. H. H. Dunlop, who was in general practice in Tangier for over 20 years, died at Oxford on November 19. He was 59 years of age.

Henry Hutchison Dunlop was born at Edinburgh in 1900, but his boyhood was spent in Girvan, where he acquired a lasting love of both sea and country. He graduated M.B., Ch.B. from Edinburgh University in 1923, and then held an appointment at the Victoria Hospital, Southend-on-Sea, after which he was in general practice in nearby Thorpe Bay from 1926 to 1928. He then went as a ship surgeon with the British India line for six years, travelling far and making many friends.

In 1935, following his marriage, Dunlop settled in Tangier, where he carried on general practice for 22 years. He gave much of his time freely to the work of infant-welfare centres and other clinics for the poorer sections of the Moorish and other populations; and he attended many of these in their own homes with endless care and patience, without thought of payment, and in conditions of the utmost difficulty for the practice of medicine.

R. G. McI. writes: Harry Dunlop was a man in whom courage and gentleness were wonderfully blended. He was unobtrusive almost to a fault, but quietly effective in all that he said and did. Patients and friends who knew him in times of stress will recall with gratitude the steadying influence of his presence. Although much of his life was spent overseas, he retained a deep love for Scotland, and his lively sense of humour was rooted in his native idiom of thought. He was a knowledgeable gardener (especially about roses), a first-class golfer, and a keen angler. On holidays in Orkney (the family home of his wife) he was the perfect fishing companion in good fortune or bad, rain or shine, speech or silence. He was greatly loved by all who knew him. His life, in its own quiet way, was a testimony to the intrinsic goodness in human nature and an adornment to the best traditions of his profession.

WALTER MESTITZ, M.D.

Dr. Walter Mestitz, paediatrician to the Mid-Sussex Hospital Group, died at the Middlesex Hospital last month. He was 63 years of age.

E. D. S. writes: Walter Mestitz was one of the many refugees from Nazi oppression who found shelter in this country and who have done such admirable work here. He qualified in Vienna and decided to specialize in gynaecology, becoming in due course first assistant to Professor Joseph Halban before going into private consulting practice, in which he was very successful and happy until the Anschluss brought his world about his ears. After a time of great suffering and anxiety, he found what he at first thought was only temporary asylum in England, but he was finally given permission to stay here though not allowed to practise. In 1941 permission to practise was granted him and he was appointed resident medical officer at the Royal Alexandra Hospital for Sick Children at Brighton. This was a very humble post for a man of his seniority and attainments, but at a time when there was an acute shortage both of senior and junior staff he was quite invaluable. He quickly became much more than an ordinary R.M.O. and was soon doing the lion's share of the work, both medical and surgical, and doing it extremely well. He really held the hospital together at a most difficult time. We who were there were deeply appreciative of what he did and knew that we could always rely on his judgment and great ability. For several years he did the greater part of the surgical work of the hospital as well as being the only resident medical officer.

When the staffing difficulties were eased after the war he acted as senior resident medical officer, but was not quite so overworked as he had been and was relieved of some of the more junior duties. With the coming of the National Health Service he was given S.H.M.O. rank and did full consultant duties as a paediatrician in the Brighton area. He was never granted full consultant status, possibly because he had no English qualification, and, though it was not in his nature to complain, his colleagues felt that, in view of his outstanding ability and the duties that he undertook, he was not very fairly treated. It was a great privilege to know and work with Walter Mestitz and to be his friend. His nobility of character, his sincerity, his great kindness and delightful wit endeared him to all who knew him. His patients, his colleagues, and the nurses loved him, and he is mourned by them all. Our warm sympathy goes to his widow, who was a sister at the Royal Alexandra Hospital, and to his son, who is also in the profession.

B. HUMPHRIES, M.B., Ch.B., D.Obst.R.C.O.G.

Dr. B. Humphries, an assistant medical officer of the public health department, Birmingham, died in the General Hospital there on November 20 at the age of 36.

Barrymore Humphries was educated at High Storrs Grammar School, Sheffield, going on to study medicine at Sheffield University, where he graduated M.B., Ch.B. in 1948. Among the hospital appointments he held were those of house-surgeon at the Royal Hospital, Wolverhampton, obstetric house-surgeon at the City General Hospital, Sheffield, and junior registrar at the Jessop Hospital for Women, Sheffield. He obtained the Diploma in Obstetrics in 1949, and, deciding to make his career in public health, joined the public health department at Birmingham in 1951.

A. J. E. C. writes: Dr. Humphries had suffered intermittent ill-health for several years, but in spite of this handicap he was a most diligent and valuable member of the staff of clinical medical officers in the Birmingham health department. He was especially well known at the Carnegie Institute maternity and child-welfare centre in Hockley, where he worked for several years, becoming very popular with both mothers and children. A patient and thorough clinician, he was especially successful with his younger visitors. He had a keen interest in medical advances, and only a short while before his death he attended an evening paediatric meeting at the Children's Hospital. Aware for a long time that his prognosis was extremely poor, Barrymore Humphries remained a charming and patient physician, a pleasant colleague, and a devoted husband and father. He leaves a widow and two young daughters.

J. A. MACKAY-ROSS, M.R.C.S., L.R.C.P.

Dr. J. A. Mackay-Ross, who practised in Chelsea, died at his home there on November 24, at the age of 61.

John Andrew Mackay-Ross was born on May 6, 1898, the son of Dr. T. M. Ross, of Chelsea. After the first world war he became a medical student at St. Bartholomew's Hospital, qualifying in 1923. Thereafter he went into practice with his father, eventually succeeding him. During the second world war he gave outstanding service as the medical officer of a first-aid post attached to the College of St. Mark and St. John in the King's Road. In the area of London in which he practised Dr. Mackay-Ross was a well-known and popular doctor, and many of his patients were among the large congregation at his funeral at St. John's Church. He leaves a widow, with whom much sympathy will be felt.

L. G. SAMUEL, M.B., Ch.B., D.P.H.

Dr. L. G. Samuel, deputy medical officer of health, Preston County Borough, was killed in a motoring accident on November 22. He was 33 years of age.

Leslie Grindlay Samuel was born on April 5, 1926, and was educated at Glasgow University, where he graduated M.B., Ch.B. in 1950. After holding a house appointment at Glasgow Royal Infirmary, he served for two years with

the R.A.F. He then returned to Glasgow, where he took the D.P.H. in 1953. He was thereafter appointed to the public-health staff of the county borough of Preston, and was promoted to the position of deputy medical officer of health in 1956.

J. S. G. B. writes: A quiet, thoughtful man devoid of malice or self-glorification, Leslie Samuel had a capacity for getting the best out of others, and with the application of his own outstanding abilities and enthusiasm there was produced a constant flow of useful contributions to the health and welfare activities of the department in which he was so universally popular. His deep religious feelings made him an active participant in church activities, especially those associated with the younger sections of the population. The future was full of promise for him, and his untimely passing is a grievous loss to his many friends and associates.

Medical Notes in Parliament

EVIDENCE BEFORE DISCIPLINARY TRIBUNALS

COMMITTEE OF INQUIRY

[FROM OUR PARLIAMENTARY CORRESPONDENT]

The proceedings before the General Medical Council relating to Dr. K. M. Fox* have precipitated an inquiry into the powers of all professional tribunals to compel the production of evidence, and in particular the use of the subpoena; have moved the Home Secretary to seek from chief officers of police an assurance that whenever they are asked to disclose evidence to a tribunal they will inform him immediately; and have deferred decisions on the disciplinary committees of the eight supplementary professions covered by the new Bill† until the inquiry has been completed.

Censure Motion in the Commons

That was the outcome of the debate which the Opposition initiated by a censure motion in the House of Commons on December 16. The broader issue of the relations between police and public was substantially removed from the scope of the debate by the announcement earlier in the day of a Royal Commission under the chairmanship of Sir Henry Willink to review the constitutional arrangements for the control and administration of police forces, including the accountability of provincial forces to Parliament.

Government and Opposition views on the complete prohibition of telephone tapping diverged hardly at all, but they were in complete contradiction on the circumstances of the Reading incident (in which the police listened on a private extension with the consent of the subscriber)—the Opposition contending that all interceptions fell within the Birkett Committee's requirement that the warrant of the Home Secretary should be required; and the Government holding that there was no parallel between "private eavesdropping" and the secret tapping of the public telephone system.

The censure motion expressed regret at the failure of the Home Secretary to ensure that no telephone conversations should be intercepted without his express warrant, and that material obtained by interception should in no circumstances be made available to any body or person whatever outside the public service; and called on the Government to carry into effect their acceptance of the recommendations in the Report‡ of the Committee of Privy Councillors [the Birkett Committee] appointed to inquire into the interception of communications.

*See *Supplement*, December 5, p. 182; and *Journal*, December 12, pp. 1316 and 1342.

†See *Journal*, November 28, pp. 1164 and 1190; and *Journal*, December 5, p. 1264.

‡*Cmnd.* 283, 1957. H.M.S.O., London.

Police Interception without Warrant

Mr. GORDON WALKER (Smethwick, Lab.), in the opening speech, rejected as dangerous the argument that there could be legitimate eavesdropping without express authority. The line must be drawn where the police were involved. They had recorded the words of a man, who knew nothing about it, with the object of incriminating him. It had been found that by the simple device of finding the right point on a telephone line other than a public exchange at which to make the interception, any policeman could make any interception without a warrant. He rejected also the argument that the Home Secretary could do nothing because he had no control over the provincial police; his authority and duty to control interceptions derived from his capacity as Secretary of State, not from his capacity as a police authority. Unless the Home Secretary accepted the responsibility for seeing that there was no official interception without his warrant, all the safeguards for the citizen were rendered nugatory.

On the second aspect, of disclosure outside the public service, he claimed that opinion was almost unanimous that the Secretary of State had been wrong. It would be hard to find more comprehensive terms than those used in the Birkett report, "We recommend that in no circumstances should material obtained by interception be made available to any body or person whatever outside the public service." The subsequent disclosure in the Reading case meant that the words of a man were secretly taken down by the police, without his knowledge, and then used in evidence where he was in jeopardy. That made the original interception much worse. It was an absolute departure from all proper police behaviour. There was another issue—the proposal in the Professions Supplementary to Medicine Bill that other private tribunals should be given the same powers as the General Medical Council. Clearly these must be limited, but that would not be enough because there were existing bodies which had the powers. An early opportunity must be taken to clear up the matter over the whole range of private tribunals.

Mr. Butler's Defence

Mr. R. A. BUTLER refused to budge at all from his contention that there was the clearest possible distinction between what had happened at Reading—a single conversation with the agreement of one of the parties, which involved no infringement of the law—and the secret interception of telephone calls of a particular individual on the warrant of the Home Secretary. He maintained that under the existing law—and in advance of the police inquiry—no Minister of the Crown had power to intervene in the daily operations of the police, and that any politician who sought to take away the independence and autonomy of the police would be the biggest enemy of personal liberty. There were many methods of inquiry which might be distasteful, but which on occasion might be necessary in the battle against crime. It would not be practicable by legislation to prohibit the police from using them, and inquiries assured him that this particular method was used very rarely.

On the use of Crown privilege to withhold the evidence so obtained, he made the point that executive interference with the processes of justice was inherently undesirable. When a court or tribunal had to try a case it was clearly desirable that as far as possible all relevant evidence should be before it, otherwise one or other of the parties, and sometimes the defendant, might be prejudiced. The document in this case (shorthand notes of the telephone conversation) did not fall easily into any of the classes for which privilege had been claimed in the past. He was advised that he would not be justified in claiming privilege for it, and he had no doubt at all that that was right. To have done so would have involved an extension of the area of privilege, which should be kept as narrow as possible. Even if privilege had been claimed, oral evidence of the conversation could have been given—and was given—by the subscriber. To have checked that would have been an inroad indeed into liberty. Future cases would have

to be judged on their merits. The General Medical Council, commenting on this one, had said it seemed most unlikely that the sequence of events would ever recur. He would think that very probable. Here came the first hint of change: he would ask chief officers of police to ensure that whenever they were asked by any disciplinary tribunal to produce evidence on subpoena they would let him know at once so that the fullest consideration might be given to the question whether the public interest involved or justified a claim of privilege.

Must Professional Tribunals be Curbed?

Then he posed the central question—Is there a case for curtailing the powers of these professional disciplinary bodies? It might be possible to provide by legislation that no such body should have power to secure the issue of a subpoena to the police. But the House must carefully consider the implications of so doing. Parliament had conferred these special powers on these bodies to protect the public. Any such proposal would require full consultation with the bodies affected. Preliminary views he had received from the General Medical Council indicated that the powers of subpoena were vital to the thorough investigation of some cases, and might be vital for the person appearing before them. Another possible approach might be to make them subject to some control—for example, making a subpoena obtainable only by leave of a Judge or Master of the High Court. The question of a claim for Crown privilege could be considered at that stage, and whether the police could properly refuse information on grounds of public policy. Such an arrangement would require legislation, but might go some way to meet the anxieties that had been expressed.

Simonds Committee

This was a most complex problem. It was necessary to keep in mind that the disciplinary tribunals had been charged by Parliament with the duty of preserving the good name and integrity of the professions; and they should not lightly interfere with these bodies, which for many years had performed their duties with fairness and efficiency. All this led him to the conclusion that a close and searching review was necessary. Therefore the Government had decided to set up a committee with these terms of reference—

"To consider to what extent and subject to what conditions subpoenas (or in Scotland citations) should be issuable to secure the attendance of witnesses and the production of documents before disciplinary tribunals; and in particular to consider whether subpoenas should be issuable to secure the production before such tribunals of evidence obtained by police officers in the course of criminal investigation; and to make recommendations."

He announced that Lord Simonds would be the chairman, and said the names of the two other members, one from England and one from Scotland, would be announced shortly. Pending their report, conclusions should not be reached on the content of the Second Schedule to the Professions Supplementary to Medicine Bill, which dealt with these matters.

Counsels' Opinions

In those two speeches lay the general arguments. But in others the General Medical Council came in for specific comment from lawyers. Mr. DINGLE FOOT, Q.C. (Ipswich, Lab.), called attention to the anomalies that would arise if a distinction was to be made and this form of evidence be used only in the courts and not before professional tribunals. If a doctor was charged with a crime in a court and was acquitted, but "telephone" evidence showed that he was guilty of serious professional misconduct, the disciplinary committee would be perfectly familiar with what had passed in court and yet would be unable to have regard to that evidence. In spite of the difficulties, it was a question of all or nothing: the evidence must be generally available in any lawful trial or inquiry, or—as he preferred on balance—be prohibited altogether.

Mr. JOHN HOBSON, Q.C. (Warrington and Leamington, Con.), said the whole integrity and standing of the medical profession, and public trust in it, depended on the way the G.M.C. carried out its duties. Justice—holding the scales between the propriety of the profession and the rights and liberties of the individual doctor—consisted of discovering the truth. That could not be done without having the evidence available. Unless the disciplinary committee had the power to inquire into matters of complaint, and the right of subpoena, they could not do their duty properly, and would be thrown back on far less satisfactory methods. The right of subpoena was not challenged when it was conferred by the Medical Act, 1950, and the reason for that was that before that Act the G.M.C. had not been able to discharge its duty of discovering the truth, because witnesses failed to turn up and the proceedings collapsed. There were important safeguards in the provision for a legal assessor—none of the decisions or advice given by the legal assessor of the G.M.C. had been reversed on appeal—and the right of appeal to the Judicial Committee of the Privy Council.

Mr. P. RAWLINSON, Q.C. (Epsom, Con.), said he hoped the inquiry would reject any suggestion for the removal of subpoena powers from the professional bodies. They had been given those powers by Parliament because discipline in those bodies was in the public interest. In the past 60 years the G.M.C. had made only 290 erasures, only one-quarter of which were due to improper or indecent conduct, such as adultery. The remainder were due to attempting or procuring miscarriages, offences of fraud and forgery, canvassing, and offences relating to drink and drugs. Since 1950 there had been only three appeals to the Privy Council, and none had succeeded.

Censure Rejected

The Attorney-General, Sir REGINALD MANNINGHAM-BULLER, winding-up the debate, said the duty which rested on the disciplinary committee was an onerous one, and in discharging it the committee acted not just in the interests of the medical profession but for the protection of the public. Parliament, he thought, was right in 1950 in thinking that the parties appearing before the body—whether to prosecute or defend—should have the right of securing the evidence they wanted by taking out a High Court subpoena, and that if they had not that right injustice might result. It was clear from the terms of reference that the right to sue out subpoenas would fall to be reviewed by the Simonds Committee. It might well be the case that, while the right to compel attendance before one tribunal was desirable, there was no need to give the same power to another.

The censure motion was rejected by 336 votes to 238.

QUESTIONS IN THE COMMONS

Inquiry into Noise

The Government, it was announced on December 10, has decided to set up a committee to examine the nature, sources, and effects of the problem of noise, and to advise what further measures can be taken to mitigate it. The MINISTER OF HEALTH, who made this announcement in answer to Mr. G. NABARRO (Kidderminster, Con.) also told him that the membership of the committee (which has still to be announced) will be made as comprehensive as possible, subject always to not making it too unwieldy. He had it in mind that it would be possible for subcommittees to examine special and technical aspects.

Mr. RONALD BELL (Buckinghamshire South, Con.) and Dr. EDITH SUMMERSKILL (Warrington, Lab.) both emphasized that the committee should report reasonably quickly, and that its recommendations should not be allowed to become abortive. Mr. WALKER-SMITH said the desirability of a report as soon as practical was fully in mind, and also the fact that it should be followed by appropriate action. He would not exclude the possibility of an interim report, but that would be a matter for the committee.

Senior Registrars

The MINISTER OF HEALTH informed Mr. L. PAVITT (Willesden, West, Lab.) that on July 1 last there were 119

time-expired senior registrars employed in the Health Service. Mr. Pavitt said that these registrars had a high degree of responsibility, and undertook major operations, yet after all these years in service they had no knowledge of the future of their jobs. They did not know whether they were to be shifted at the end of their existing year. As a result, they were left in a state of considerable uncertainty. Would the Minister consider taking action to resolve their difficulties? Mr. WALKER-SMITH replied that action had been taken. Jointly, with the Joint Consultants Committee, they had set up a working party to study the principles of staff structure in the hospital service, with particular reference to this problem. Meanwhile regional hospital boards and boards of governors had been asked to extend the contracts of senior registrars who had completed the normal tenure of their posts.

Mr. K. ROBINSON (St. Pancras North, Lab.) asked how the number of 119 compared with that of the previous twelve months, and what effect the once-for-all arrangements had had on the limited number of permanent appointments announced a year ago. Mr. WALKER-SMITH said the number was five fewer than previously. On the second point, there had been 23 proposals, of which 19 had been approved.

Publication of Doctors' Names

Mr. M. LIPTON (Brixton, Lab.) asked the Minister on December 14 if he would require publication of the names of doctors fined by executive councils for neglect of duty, Mr. WALKER-SMITH: While all practices and procedures are kept under review, I do not at present think it would reflect the balance of the public interest to propose that the existing arrangements under which doctors enter into contracts with executive councils should be amended in this way.

Mr. LIPTON asked if the Minister would not agree that it must be a bad case before a doctor was fined in this way? Why did he still maintain that on balance it was in the public interest that a doctor who failed in his duty to his patients—for example, in refusing to visit a dying patient—should have his name shielded by a secret tribunal? Mr. WALKER-SMITH told him that they were not necessarily serious cases which came within the ambit of this procedure whereby doctors have part of their remuneration withheld. There were some which were technical and relatively trivial offences, where the harm done to a man's professional reputation would be out of proportion to the gravity of the offence with which he was charged.

Review of Medical Education

Mr. K. ROBINSON asked what was the nature of the last comprehensive inquiry or review of medical education; and when it took place. Mr. WALKER-SMITH stated that since the Committee on Medical Schools under the chairmanship of Sir William Goodenough reported in 1944 the General Medical Council in 1947, and again in 1957 after comprehensive review, published revised recommendations on the medical curriculum.

Mr. ROBINSON: Does the Minister not think the time has come for a careful and perhaps more dispassionate examination, to discover the extent to which medical education is in line with current concepts of medicine and with the requirements of the Health Service? Will he give the matter some thought? Mr. WALKER-SMITH said this was primarily a matter for Viscount Hailsham, Lord President of the Council. Mr. Robinson could be assured there was constant thinking about these matters, independently of setting up specific inquiries such as the Goodenough Committee.

Toxic Sprays Investigation

Colonel TUFTON BEAMISH (Lewes, Con.) asked the Minister of Agriculture, Fisheries, and Food, if he would announce the names of the small group of scientists who were to examine the use made of toxic sprays in agriculture and to make proposals as to whether more research was necessary; and what their terms of reference would be.

Mr. J. HARE stated that the Minister for Science and he, together with the Secretary of State for Scotland and the Minister of Health, were still considering the composition of this group, but they had in mind that it would consist of about eight scientists comprising, among others, his chief scientific advisers on agriculture and on food, the director of the Plant Pathology Laboratory, and persons nominated by the Medical Research Council, the Agricultural Research Council, the Department of Scientific and Industrial Research, and the Nature Conservancy. The terms of reference would be: "To study the need for further research into the effects of the use of toxic chemicals in agriculture and food storage, and to make recommendations."

Risks of Carcinogenesis

Mr. JOHN FARR (Harborough, Con.) asked the Minister of Health what investigations had been made into the possibility of certain toxic sprays used in agriculture causing cancer; and with what result. Mr. WALKER-SMITH replied that, in the investigations on the toxic effects of chemical sprays used in agriculture being sponsored by the manufacturers of the products and the Medical Research Council and other organizations, consideration was always given to the possibility that these substances might cause cancer. A few substances had been condemned in the United States, but the great majority proposed for use showed no evidence of such properties.

Mr. FARR said that research abroad had shown that certain of these weed-killers could cause thyroid cancer in rats. Would the Minister of Agriculture appoint a commission to inquire into this and other aspects of toxic sprays? Mr. WALKER-SMITH said the suggestion would be noted, but he would like to make it clear that no toxic sprays had been condemned in this country as carcinogenic, and those identified as such in the United States had not found their way on to the British market.

D.D.T. and Blood Disorders

Mr. FARR also asked what investigations had been made into the possibility of D.D.T. and some of its solvents used in agriculture causing leukaemia, aplastic anaemia, jaundice, and other blood disorders; and with what result. Mr. WALKER-SMITH said that experimental studies undertaken under the auspices of the Medical Research Council and by other workers had provided no evidence that blood disorders could be produced by D.D.T. He understood that manufacturers of this substance avoided the use of solvents which might have undesirable effects on the blood. Occasional reports in medical literature, he added, had attributed blood diseases to D.D.T., but the cause of illness had invariably been poorly substantiated in those cases.

Accident Services

Mr. J. CRONIN (Loughborough, Lab.) asked what consideration the Minister had given to the *Memorandum on Accident Services, 1959*, published by the British Orthopaedic Association, and if he was aware that the accident services of Great Britain were inadequate in organization, staffing, accommodation, and training of medical personnel.

Mr. WALKER-SMITH replied that he had sought the advice of the Standing Medical Advisory Committee, who had set up a subcommittee to consider the provision of traumatic and accident services.

Redundant Tuberculosis Beds

Mr. A. WOODBURN (Clackmannan and Stirling, East, Lab.) asked the Secretary of State for Scotland on December 15 how many beds had become available for other purposes as a result of the decrease in the need for tuberculosis treatment; and whether these were being fully utilized for maternity, geriatric, and other urgent needs. Mr. T. GALBRAITH, Joint Parliamentary Under-Secretary, said that between June, 1958, and June, 1959, some 900 tuberculosis beds became redundant. About 700 had already been put to other uses, over half being used for the elderly sick. Most of the remainder were closed only temporarily while arrangements were being made for their future use.

Mr. WOODBURN asked the Minister, in view of the desperate urgency for this provision and the complaints made about hardship, whether he could not speed up this transition of the beds from their former use to meet these other urgent needs. Mr. GALBRAITH suggested that if Mr. Woodburn looked at the figures he would see that they had not been doing too badly. He had a great deal of sympathy for Mr. Woodburn's point of view, but, owing to structure and remoteness, some of the hospitals were not suited to the purpose he had in mind.

Vivisection Inquiry Refused

Mr. L. M. LEVER (Ardwick, Lab.) asked the Home Secretary if he would set up a committee of inquiry into the use of animals for experiments. Mr. R. A. BUTLER: No. I do not consider that there is need for an inquiry.

Alcohol and Driving

Mr. J. RANKIN (Govan, Lab.) asked the Minister of Transport on December 16 if he was aware that the official committee on road users had reported that small amounts of alcohol taken by drivers of motor vehicles impel them to take greater risks than they would normally take, and make them less efficient in dealing with hazardous situations which they may consequently precipitate. What action did he propose to take to deal with this problem in the public interest?

Mr. J. HAY, Joint Parliamentary Secretary to the Ministry, said he presumed that Mr. Rankin referred to a memorandum in which the Medical Research Council recently published an account of laboratory experiments bearing on the effect of small doses of alcohol on a skill resembling driving. The conclusions were the responsibility of the research team concerned, and did not in the Ministry's view provide a basis on which legislative proposals could be framed for presentation to Parliament. They proposed to continue discussions on the general issue with the Medical Research Council.

Vital Statistics

Favourable Statistics in Third Quarter

During the quarter ended September 30, 1959, the infant mortality rate (deaths of children under 1 year of age) in England and Wales was 18.7 per 1,000 live births—1.5 per 1,000 lower than for the third quarter of 1958 and 8 per 1,000 lower than for the corresponding quarter 10 years ago.

Notifications of acute poliomyelitis during the third quarter, at 447, were not much more than half the notifications in the corresponding quarter of the previous year.

Deaths from transport accidents numbered 1,632. This was 124 more than in the corresponding quarter of 1958. The 499 deaths of motor-cyclists (including passengers) were one-third more than in the September quarter of 1958.

The weather between June and September was exceptionally good. The daily mean temperature was 2.3° F. above the average, the rainfall was 47% of the average, and the sunshine was 133% of the average.—*Registrar-General's Quarterly Return*, No. 443.

London's Health

The report of the London County Council's medical officer of health records an increase in the birth rate in 1958. The figure of 16.8 per 1,000 population was the highest since 1948. Over 8,000 births in London were illegitimate—that is, 9.9% of the total live births. This percentage has risen from 7.1 in the last four years, while the national figure has remained steady at about 4.8. Dr. J. A. Scott, the county medical officer, remarks that there is a greater risk of illegitimacy in London because proportionately fewer of the potential mothers in the population are married. But he attributes some part of the excess "to the facilities London can offer to the unmarried mother—antenatal care, anonymity, and support from moral welfare organizations."

Among the other facts recorded in the county medical officer's report are an increase in deaths from cancer by about 14% in the last 10 years. The male death rates from lung cancer (adjusted for age) were highest in the boroughs of Bethnal Green, Finsbury, Shoreditch, Islington, St. Pancras, Southwark, and Bermondsey.

On the subject of deaths attributable to smog, Dr. Scott writes: "So far, in the history of London smogs there does not seem to have been an incident causing excess deaths which has not also been accompanied by low temperatures . . . it may be possible in due time to make a statistical estimation of the relative importance of cold and pollution in their consequences."

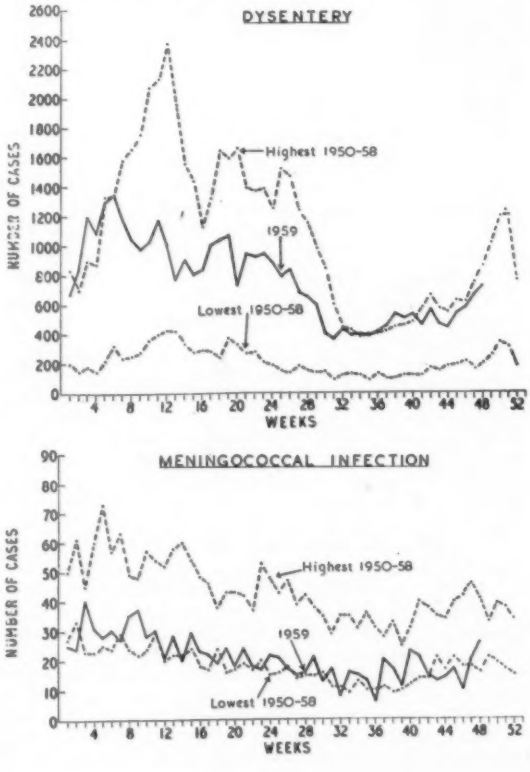
The London ambulance service received a record number of emergency calls—an average of 272 a day. Friday was the busiest day of the week, and December the busiest month. Between 2 p.m. on Christmas Eve and 2 a.m. on Christmas morning, 1958, there was an emergency call every 105 seconds.

Diphtheria in London

The chairman of the health committee of the London County Council, answering a question on December 15 about recent outbreaks of diphtheria in London, said that the total number of children found by swabbing to be infected with the diphtheria bacillus was 111 in Finsbury and Islington and 59 in Camberwell.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1950–8 are shown thus ------, the figures for 1959 thus ———. Except for the curves showing notifications in 1959, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **December 5** (No. 48) and corresponding week 1958.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1959					1958				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	5	4	4	0	1	7	2	8	0	2
Dysentery ..	723	96	153	7	9	1,098	95	166	20	1
Encephalitis, acute	1	0		0		4	0		0	
Enteric fever:										
Typhoid ..	3	1	0	0	7	3	2	0	0	1
Paratyphoid ..	1	0	3(B)	0	2(B)	5	1	3(B)	0	
Food-poisoning ..	190	39	7	1		236	17	9	1	1
Infective enteritis or diarrhoea under 2 years				11	24				16	27
Measles*	1,110	26	22	13	69	6,910	398	190	32	365
Meningococcal infection	26	4	6	0		16	0	14	1	
Ophthalmia neonatorum	20	0	4	0		26	8	7	0	
Pneumonia† ..	305	15	210	5	1	407	40	197	8	
Poliomyelitis, acute:										
Paralytic ..	11	3	0	0	4	50	1	3	1	6
Non-paralytic ..	2	0	1			19	0			
Puerperal fever§ ..	156	19	9	1	1	184	23	11	0	
Scarlet fever ..	1,418	90	131	28	21	1,164	82	127	23	48
Tuberculosis:										
Respiratory ..	430	50	75	18		480	45	116	15	
Non-respiratory	50	9	8	5		65	14	10	4	
Whooping-cough	739	53	187	7	87	724	29	78	90	106

DEATHS	1959					1958				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	10	0	1	0	1	7	0	0	0	1
Influenza	19	2	0	0	1	11	0	2	2	1
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		1	0				0	2		
Pneumonia ..	518	35	20	28	6	533	42	19		10
Poliomyelitis, acute	3	0		0	0	8	0		0	0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	87	5	3	4	3	111	8	8	0	5
Non-respiratory		0	1	0	0		1	0	0	0
Whooping-cough	0	0	0	0	0	1	0	0	0	0
Deaths 0–1 year ..	294	28	22	10	9	327	27	27	4	10
Deaths (excluding stillbirths) .	9,945	785	549	174	167	10,403	859	532	129	149
LIVE BIRTHS .	12,877	1092	870	228	356	13,396	1167	1013	197	307
STILL-BIRTHS	258	23	17			327	33	22		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Public Health Laboratory Service

The Public Health Laboratory Service Bill received its first reading in the House of Lords on December 9. Its purpose is to set up a P.H.L.S. Board to administer the Service, subject to directions from the Minister of Health. The Board will have a medical chairman and nine other members. The members (who will be unpaid) will include two appointed after consultation with the Medical Research Council, two bacteriologists, and two medical officers of health. At present the Medical Research Council administers the Service for the Minister of Health.

William Gibson Research Scholarship for Medical Women

Applications are invited for this scholarship from women who are British subjects and who hold a registrable medical qualification. The scholarship, which is normally awarded for two years but which may be extended for a third year, is for £200 p.a. In choosing the scholar, the council of the Royal Society of Medicine will be guided by the research work already done or contemplated by candidates. It is expected that a candidate will hold a recognized appointment and that the scholarship will be a useful aid to research either in the United Kingdom or abroad. The next award will date from October 1, 1960, and applications must be received by the Society by May 1, 1960. They should be addressed to the Secretary, Royal Society of Medicine, 1, Wimpole Street, London, W.1, and should give details of professional training received, appointments held, research work undertaken or contemplated, and the names of two referees.

Paediatric Microbiology

Applications are invited by the department of paediatrics, Western Reserve University, School of Medicine, Cleveland, Ohio, to join a two-year training programme in paediatric microbiology. The programme is being run in collaboration with the department of preventive medicine, and the Babies and Children's Hospital of University Hospitals of Cleveland, and is supported in part by the United States Public Health Service. Stipends starting at $5,000 a year are available, and details may be obtained from Dr. R. J. WEDGWOOD, Department of Pediatrics, 2103, Adelbert Road, Cleveland, 6, Ohio, U.S.A.

King Edward's Hospital Fund for London

At a meeting of the Fund's general council on December 11 it was reported that grants made during the year amounted to £260,000, and it was resolved that about £391,000 be set aside for grants to hospitals and convalescent homes, and for the maintenance of various services and educational activities in 1960. During the year over 2,550 members of hospital staffs had attended courses of more than a fortnight's duration, and in some cases of one, two, and three years' duration, at the Fund's three staff colleges and school of catering.

British United Provident Association

In its annual report for the year ended June 30, 1959, the association discloses that for the first time its subscription income has topped £3m.; nearly 85% of it was absorbed by claims and rather less than 10% by administration expenses. During the year there were nearly 40,000 new registrations, bringing the total protected by B.U.P.A. to 750,000; during its first six months 2,894 subscribers joined the new General Practitioner Scheme introduced in January, 1959.

Royal Medical Benevolent Fund

The Fund's *123rd Annual Report for the Year 1958* reveals that because of the ever-increasing number of requests for help the year's accounts show a deficit of £3,895. A bequest from the late Mr. J. T. M. GIFFEN has enabled the Fund to purchase a house in Putney for conversion into

five flats for "indigent doctors," and applications for residence in them are invited. The Fund's address is 37, St. George's Road, Wimbledon, London, S.W.19 (Wimbledon, 1792)

The New St. Thomas's

Work on the new St. Thomas's Hospital is due to begin next year, and this model of the plans—slightly modified from those shown in the *Journal*, p. 115, January 11, 1958—shows how the hospital will appear from the Waterloo Station side.

[*Central Press Photos, Ltd.*

Transatlantic Telephone Conference

The Glasgow Division of the British Medical Association held a highly successful telephone conference with Dallas, Texas, on December 3, in the Maurice Bloch Lecture Theatre of the Royal Faculty of Physicians and Surgeons of Glasgow.

About 280 doctors attended, and the members of the Glasgow panel were: Professor W. A. MACKEY (chairman), Dr. G. J. AITKEN, Dr. T. SEMPLE, and Mr. G. SMITH. The chairman of the Dallas panel was Professor J. S. CHAPMAN, assistant dean and professor of medicine, University of Texas, and South West Medical School, Dallas, Texas. Discussion and diagnosis of the two case histories presented lasted 59 minutes and both Smith, Kline and French Laboratories, Ltd., and the Post Office engineers are to be congratulated on the excellence of the technical arrangements. To the audience, at least, there were no obvious hitches. Perhaps the lower pitch of the American doctors' voices came over the loudspeakers better, but so far as arriving at the correct diagnosis was concerned honours, as Professor Mackey said at the end, were about even.

Imperial Cancer Research Fund

A presentation dinner was given to Professor GEOFFREY HADFIELD at the Royal College of Surgeons on December 8.

Sir CECIL WAKELEY, chairman of the Fund's council, was in the chair, and presented Professor Hadfield with an inscribed volume of the *Shorter Oxford Dictionary* and a Waterman pen and pencil on behalf of the council as a small memento of their esteem and friendship over so many years while Professor Hadfield was director of the clinico-pathological research laboratories of the Fund.

Marie Curie Memorial Foundation

At the annual meeting earlier this month it was announced that the Foundation's voluntary income has exceeded £300,000 for the first time and has grown from £85,194 in 1954 to £300,500 at June 30, 1959. Seven homes for cancer patients have been opened, the eighth purchased, and the search continues for two further properties. Area welfare grants now cover 62 areas—virtually a complete coverage of the United Kingdom. Personal applications for cancer educational leaflets have risen from 371 in 1957 to 45,496 during the current year.

Noise

The Government has decided to set up a committee to examine the nature, sources, and effects of the problem of noise, and to advise what further measures can be taken to mitigate it. The membership of the committee will be announced later.

Physiologists in Himalayas

It is hoped that an expedition led by Sir EDMUND HILLARY will spend nine months in the Himalayas next year studying human reactions at high altitudes. Among the physiologists accompanying the expedition will be Dr. GRIFFITH PUGH, of the National Institute of Medical Research.

COMING EVENTS

Leeds Neurological Sciences Colloquium, 1959–60.—On Tuesdays, 5.15 p.m., January 5–March 29, in the Little Hall, General Infirmary, Leeds. Details each week in *Journal* diary.

Bone and Tooth Society.—Meeting on "Radioactive Materials and the Skeleton," January 13, 11 a.m., Cuthbert Wallace Room, Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2.

"Dynamics of Alcoholism"—This film will be shown at the Medical Society of London, 11, Chandos Street, W.1, January 19, 8 p.m., by the Society for the Study of Addiction.

Royal Medico-Psychological Association.—Maudsley Bequest: Two-day Lecture Course at the Royal Society of Medicine, 1, Wimpole Street, London, W.1, February 8 and 9, 1960. Details from the Secretary, Royal Medico-Psychological Association, 11, Chandos Street, Cavendish Square, London, W.1.

M. D. Anderson Hospital and Tumor Institute University of Texas.—14th annual symposium on fundamental cancer research, "Cell Physiology of Neoplasia," February 25–27, 1960. Details from Editorial Office, University of Texas M. D. Anderson Hospital, Texas Medical Center, Houston, 25, Texas, U.S.A.

4th International Goitre Conference.—The conference will now be held at Church House, Westminster, July 5–8, 1960, and not, as previously arranged, at the Royal College of Surgeons. Details from Mr. SELWYN TAYLOR, The Royal Society of Medicine, Dering Yard, 67c, New Bond Street, London, W.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Tuesday, December 29

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—At Edward Lumley Hall, 3 p.m., Holiday Lecture for Schoolchildren by Sir Ernest Finch: Romance of Surgery.

Wednesday, December 30

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—At Cuthbert Wallace Lecture Theatre, 3 p.m., Holiday Lecture for Schoolchildren by Professor Gilbert Causey: Importance of Being the Right Size.

Thursday, December 31

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—At Cuthbert Wallace Lecture Theatre, 3 p.m., Holiday Lecture for Schoolchildren by Miss Jessie Dobson, M.Sc.: Curiosities of Natural History.

Friday, January 1

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3 p.m., Holiday Lecture for Schoolchildren by Dr. W. E. Swinton: What Did Darwin Do?

Saturday, January 2

MIDLAND THORACIC SOCIETY.—At Birmingham Medical Institute, 3 p.m., short papers. Dr. James T. Hutchison: Chorion-epithelioma in a Male; Dr. J. Morrison Smith: Reactions to Chemotherapy; Mr. Eric G. Dolton: Two Cases of Cardiac Injury.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Billingham.—On November 29, 1959, to Margaret and John Billingham, of Tilford, Surrey, a second son—Graham Torquil.

DEATHS

Burstal.—On December 6, 1959, Edward Worsley Burstal, M.R.C.S., L.R.C.P., of the White House, Lutterworth, near Rugby, Warwicks.

Hardy.—On December 6, 1959, at Cranford Kenilworth, Capetown, South Africa, William Edmund Hardy, M.R.C.S., L.R.C.P., Colonel, late R.A.M.C., aged 93.

Hyatt.—On December 8, 1959, at his home, Southwell, Trull, Taunton, Som., James Wynn Hyatt, M.R.C.S., L.R.C.P., Colonel, late R.A.M.C., retired.

Lattey.—On December 7, 1959, at Ambrook, Rousdown Road, Chelston, Torquay, Devon, Richard Arthur Lattey, M.B., Ch.B., F.F.A.R.C.S.

Lawrie.—On December 7, 1959, Norman Risborough Lawrie, Ph.D., M.B., Ch.B., of 175, Huntingdon Road, Cambridge.

Rankin.—On October 15, 1959, in hospital, Alexander Douglas Rankin, M.B., Ch.B., D.P.H., of 182, The Broadway, Cullercoats, Northumberland, late of View Road, Keighley, Yorks, aged 64.

HEALTH CENTER LIBRARY

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Corticosteroids in Pulmonary Tuberculosis

Q.—*What is the action of cortisone on pulmonary tuberculosis lesions when given in conjunction with chemotherapy ?*

A.—Early experimental work suggested that the administration of corticosteroid drugs to patients with tuberculosis might result in disastrous deterioration.[1] Early clinical reports also emphasized that the administration of these drugs for conditions other than tuberculosis might result in the lighting up of a latent tuberculous focus.[2] It was probable that these unfortunate results were due to a lowering of the body's defences by the drug. However, when effective anti-tuberculous chemotherapy was given, preliminary trials suggested that no exacerbation of tuberculosis resulted, and patients who were very ill seemed to improve more rapidly than would have been expected with chemotherapy alone.[3] Nevertheless, the situation remained controversial until a carefully controlled trial was carried out by the Research Committee of the Tuberculosis Society of Scotland, whose preliminary report has been published.[4] This trial showed that in the group treated with prednisolone in addition to chemotherapy clinical improvement was more rapid, especially in those acutely ill, and the erythrocyte sedimentation rate fell more rapidly. Radiographic improvement was significantly hastened over a six-months period, most of the advantage to the prednisolone-treated group occurring in the first two months of treatment. The prednisolone group received this drug for the first three months of treatment. By six months the advantage to the prednisolone group was very much less, and it seemed likely that, with the further passage of time, the difference between the two groups would tend to disappear. It is probable that the final report on the trial may show that the prednisolone has a definite effect in hastening improvement in the early stages of chemotherapy but has little long-term advantage. The use of corticosteroids is probably justified in patients admitted severely ill, mainly on humanitarian grounds but sometimes as a life-saving measure. In desperately ill patients these drugs may sometimes ensure survival by diminishing toxicity sufficiently to keep the patient alive until the anti-tuberculous drugs can take effect. Corticosteroid drugs should never be given to patients unless it is reasonably certain that their organisms are sensitive to the chemotherapy used.

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Diagnosis of Addison's Disease

Q.—*Is the estimation of 17-oxyhydrocorticosteroids in the urine more reliable than the estimation of 17-ketosteroids in the laboratory diagnosis of Addison's disease ?*

A.—Both 17-hydroxycorticosteroids and 17-ketosteroids are excreted in diminished amounts in Addison's disease. Techniques in common use for estimating 17-hydroxycorticosteroids[1 2] measure mainly the metabolites of cortisol, a compound which is solely of adrenal origin. The urinary 17-ketosteroids, however, are derived from several sources, from adrenal androgens, from cortisol, and, in the male, from testosterone also. The 17-hydroxycorticosteroids might therefore be expected to be the more reliable guide. In fact the excretion of both 17-hydroxycorticosteroids and 17-ketosteroids may be only slightly less than normal in Addison's disease. In such cases one may suppose that the remnant of functional adrenal tissue is maximally stimulated by endogenous A.C.T.H. Furthermore, low excretions of 17-hydroxycorticosteroids and 17-ketosteroids are found also in hypopituitarism and in anorexia nervosa. A more reliable diagnostic guide is therefore the measurement of 17-hydroxycorticosteroids and 17-ketosteroids during the administration of A.C.T.H.[3] A failure to respond to exogenous A.C.T.H. indicates primary adrenal failure.

A general discussion of the problems of testing adrenocortical function was presented in a leading article in the *Journal*.[4]

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Incompatibilities of Codeine Salts

Q.—*What are the incompatibilities of codeine salts ? Would a fluid mixture containing the following be compatible : ephedrine hydrochloride 6 gr. ; sodium phenobarbitone 12 gr. ; syr. codeine phosphate 18 dr. ; tinct. belladonna 3 dr. ?*

A.—Codeine salts are incompatible with bromides, iodides, salts of heavy metals, and alkalis. Solutions of codeine phosphate are acid to litmus.

Codeine phosphate, ephedrine hydrochloride, and the alkaloids of belladonna are all more soluble in acid than in alkaline solution, whereas sodium phenobarbitone is more soluble in alkaline solution. There is thus a theoretical possibility of incompatibility between these compounds. In practice the formula quoted has given a bright clear solution which has shown no precipitation after eleven days. It is slightly alkaline to litmus.

Reheated Dripping

Q.—*Is there any foundation for the statement, made recently in the lay press, that reheated dripping used in deep frying was a cause of cancer and coronary thrombosis ?*

A.—The changes which occur when dripping used in deep frying is repeatedly reheated must be very complex and variable. There is no clear evidence that fats treated in this way cause cancer in man. The continuous reheating of fat will destroy some of the unsaturated fatty acids. If coronary thrombosis is caused by deficiency of essential unsaturated fatty acids, then the use of reheated fat might be considered as a causative factor for this disease. The ill effect could possibly be overcome by adding oils, such as corn oil, which contain essential fatty acids to the diet.

Pin-holes in a Cigarette

Q.—*I have been told that two pin-holes made about ¼ in. (1.25 cm.) from the mouth end of a cigarette lowers the combustion temperature by 60% and that the inhalation of tar and injurious products is substantially reduced. Has this any scientific basis ?*

A.—The question appears to be based upon experimental work done at University College Hospital Medical School and reported by C. N. Smyth.[1] This work showed that with holes about ¼ in. from the mouth end of a cigarette the final temperatures in the stub and of the emergent smoke were reduced by about 60° C. The cooling effect of the air drawn in through the holes also prevented a great deal of the smoke condensed in the stub from volatilizing and thus joining the smoke in the final stages of smoking. It was stated that this reduces the total "tar" by 60%.

The statement in the question that the combustion temperature is lowered by 60% is meaningless. It is probable that the surface temperature of the hot end is reduced somewhat, but it has been established that in the hot zone of a smoking cigarette the temperature is

remarkably constant at 650° C., and rises about 50° C. during suction.[2] The term "tar" is often employed in discussing smoking as if this material were something different from and separable from "smoke." The truth of the matter is that the whole of the particulate matter in tobacco smoke can be condensed to a "tar" and that, because of the very small size of the initially formed droplets, it is of remarkably uniform composition.[3] Because of confusion in the use of the term "tar" it is recommended that the term "smoke condensate" be employed to replace it.

Many ideas have been proposed for reducing "harmfulness" and "injurious products" in tobacco smoke. Several hundred compounds are known to be present[4] and some of these are known to have definite biological effects.[5] Whatever proposals are made, it is evident from the nature of smoke that successful reduction of the effect of smoking can be achieved only by taking in less smoke. The use of pinholes in the cigarette is one method of doing this.

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French Cigarettes and Lung Cancer

Q.—*French cigarettes do not cause yellow tobacco-stains on the hands. Is this due to absence of tarry substances and nicotine from French cigarettes? Is the incidence of lung cancer among French cigarette-smokers lower than among British smokers?*

A.—This question cannot be answered simply. The amount of staining of skin by smoke is affected by the type of smoke and by the habit of the smoker in handling his cigarette. The suggestion that there are no "tarry substances" and nicotine in the French brand of cigarettes is definitely wrong. The amounts may be greater or less than in other brands.

The incidence of lung cancer in France is lower than in this country in the ratio 140/461, but so also is the consumption of cigarettes in the ratio 585/1,378.[1] It has been demonstrated that the incidence of this disease is approximately proportional to the amount smoked, so French cigarettes smoked in France may be somewhat less carcinogenic than British cigarettes smoked in Britain, but many other factors are also likely to contribute to the difference. These may be related to other differences in smoking habits—for example, the amount of the cigarette smoked—or they may be entirely independent—e.g., atmospheric pollution and occupational exposure.

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Inheritance of Porphyria

Q.—*Three members of a family have porphyria. Which of many relatives should be warned against taking sulphonamides or barbiturates in order to prevent precipitating the complaint?*

A.—Acute intermittent porphyria is essentially due to a dominant gene,[1] or perhaps one of two dominant genes if, as seems probable, the South African form is distinct.[2] The chance of a relative being susceptible decreases as the relationship becomes more remote. Excluding fresh mutation, it is 1 in 2 for first degree relatives of the index cases (first degree relatives include children and brothers and sisters), 1 in 4 for second degree relatives (such as grandchildren and nephews and nieces), and 1 in 8 for third degree relatives. But a full family study would help to indicate the part of the family at risk.

It is claimed that after childhood all those susceptible to the South African variant of the illness may be detected by the presence of uroporphyrin in the faeces or in the urine. In the form reported from Sweden and commonly seen in this country,[3] many of those susceptible, but not all, may be detected by the presence of porphobilinogen in the urine. There is no doubt that barbiturates may precipitate attacks, and the sulphones have also been implicated, but this is not the case so far as I know for sulphonamides.

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Congenital Osteogenesis Imperfecta

Q.—*A young, healthy woman was recently delivered of a full-term baby suffering from fragilitas ossium. There is no history of it in either her or her husband's family. What are the chances of this couple producing healthy offspring?*

A.—Osteogenesis imperfecta tarda is due to a dominant mutant gene, but the genetic status of severe congenital osteogenesis imperfecta is not fully known. Assuming that this case is the first clinical appearance of a dominant mutation, the chances of this couple producing healthy offspring are excellent. Only one consecutive series is available on which to base an empirical risk.[1] In this series 6 patients had 19 brothers and sisters, all of whom were unaffected.

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Total Absence of Hair

Q.—*Two paternal aunts and two paternal uncles and the paternal grandfather of an expectant mother were all born with no hair on the head, no eyebrows, and no eyelashes. What chance has her baby of being born with the same condition? Is it due to a recessive gene?*

A.—Total absence of hair, without other evidence of ectodermal abnormality, is a rare condition. But there are several reports of more than one member of a family affected.[1 2] There is probably more than one clinical type, and more than one mutant gene may be responsible. In some families the pattern of inheritance is that of a dominant gene and in others that of a recessive gene. In this family it is probable that a dominant gene is responsible. Assuming that the woman herself shows no signs of the condition the chance that her baby will be affected is not great.

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Correction.—In the paper on chronic bronchitis by Dr. J. McC. Murdoch and his colleagues (December 12, p. 1277) the word "inactive" should have appeared instead of "active" in the second line under Table VII (p. 1281).

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